

was 27,300/c.mm of blood with an eosinophilia of 54 per cent His blood pressure was normal All this again confirmed the diagnosis of bronchial asthma Next morning the respirations became very deep and rapid and central pneumonia was suspected Skiagram of the chest was normal At this time patient's father gave history that the child did not pass any urine for last 36 hours and gave a history of acute nephritis a year ago On catheterisation, 2 ozs of urine could be obtained and it showed large amount of albumen, plenty of red blood cells, pus cells and many granular and hyaline casts Blood examination showed Total non-protein nitrogen 150 mgms and urea nitrogen 400 mgms/100 c.c blood

Out of 4 cases of difficulty in breathing, 2 cases had oedema of glottis, which was discovered post-mortem

*Gastro-Intestinal Symptoms*—These are often present and may completely dominate the clinical picture—the visceral uraemia of older authors Vomiting may occur on empty stomach or after any meal It may be almost continuous and uncontrollable As a result of continuous vomiting, abdominal muscles may become tender and painful and it might simulate an acute abdomen In the present series, 2 cases were admitted as acute abdomen—one was operated as a case of chronic appendicitis He developed haematemesis and melaena and post-mortem revealed it to be a case of nephrosclerosis In the other case, uraemia was suspected from drowsiness and high blood pressure Blood examination showed total non-protein nitrogen 300 mgms and urea nitrogen 150 mgms per 100 c.c of blood

Table 10 Gastro intestinal symptoms in uraemia

Gastro-intestinal symptoms.	No of Cases
Nausea and vomiting	20
Diarrhoea with or without blood	11
Pain in abdomen	7
Stomatitis and dry tongue	7
Constipation	6
Persistent hicough	5
Ammoniacal odour	3
Total No with gastro intestinal symptoms	32

*Oedema*—Out of 98 cases, 50 cases had generalised anasarca, often starting as puffiness of face, oedema of feet extending to scrotum or vulva, sacral region, glottis, ascites etc Hydrothorax was present in 5 cases only

Oedema of glottis is a rare but very dangerous complication It may develop while subcutaneous oedema is not very marked Early symptoms are pain in the throat and dysphagia, later difficulty in phonation might occur The danger signal is the appearance of dyspnoea and cyanosis Two cases developed oedema of glottis One patient complained of choking feeling in the throat and dysphagia He had no external oedema Oedema of glottis was discovered post-mortem The second case was admitted in a very low condition and expired after a few hours Here also oedema of glottis was discovered during post-mortem

Oedema associated with uraemia may be of two pathogenetically distinct varieties viz nephritic and cardiac. Out of 98 cases, 18 cases had congestive cardiac failure adding to oedema of nephritic origin.

**Genito-Urinary Symptoms**—Nothing was mentioned as regards these symptoms in 71 cases. The remaining 27 cases showed the following symptoms

Genito-urinary Symptoms	No. of Cases
Oliguria or anuria	22
Increased frequency	4
Frank haematuria	3
Total	27

In all the 98 cases in the present series, amount of urine became less towards the end and in some of them complete anuria set in. In the above table, only those cases are included, who had these symptoms on admission or in whom these symptoms were predominant. Cases of microscopic haematuria have not been included in the above table.

**Haemorrhages**—Bleeding is quite common in uraemia and it might occur anywhere in the body. Combination of dyspnoea of a hissing character in a drowsy patient with bleeding gums is a very characteristic clinical picture of terminal stages of uraemia. In the present series of 98 cases, 28 cases had haemorrhagic manifestations in one or more places as shown below

Site of haemorrhage	No. of Cases
Retinal	12
Stomach—haematemesis	7
Lungs—haemoptysis	4
Gums	4
Rectum	4
Nose—epistaxis	1
Total No. with haemorrhages	28

Cases of haematuria have not been included in the list of haemorrhages. In this series 4 cases had haemorrhages at more than one place—one case had haemoptysis, another haematemesis, and the third, bleeding from the gums, in addition to retinal haemorrhages. One case had haemoptysis and haematemesis both. Haemoptysis was present in 4 cases and this was not due to pulmonary tuberculosis as verified post-mortem.

**Skin Eruptions**—Notes were very scanty as regards skin eruptions. In uraemia, skin has a peculiar yellowish brown tint in long standing cases and there is marked dehydration. Pruritus is a rather common symptom. There was no mention about this symptom in any notes. Uraemic eruptions were first described by Huet, who found them in one-sixth of uraemic patients. They may be erythemas of papular, vesicular, pemphigoid or haemorrhagic type or pruritus with urticarial, eczematoid or licheniform lesions. Purpura may occur. Out of 98 cases, mention was made about this symptom in 3 cases only and they were loosely described as "skin eruptions," "scaly rash," "dermatitis," "impetigo," etc.

**Retinal Examination**—Out of 17 cases examined, 12 cases had changes of albuminuric neuro-retinitis, consisting of papilloedema of the disc, exudates and flame shaped haemorrhages, thinned out arteries with periarterial exudates and engorged veins. These changes are very important from prognostic point of view as they invariably signify very bad prognosis. Out of the remaining 5 cases examined ophthalmoscopically, 2 cases showed retinal arterio-sclerosis, 1 case showed glaucomatous cupping, and 2 cases did not show any changes.

**Temperature**—Temperature in uraemia is usually subnormal. However febrile episodes are not at all uncommon as a result of complications. Out of 98 cases, 50 cases had normal or subnormal temperature. Out of 48 cases with elevated temperature, 30 cases had some complications like broncho-pneumonia, empyema, parotitis, cellulitis, gangrene, pericarditis etc., to account for the rise of temperature. Rise of temperature was common after convulsions which occurred in 9 cases in the present series. There was no cause to account for the rise of temperature in the remaining 18 cases.

**Laboratory Investigations—Blood count**—Anaemia is usually of microcytic hypochromic type, as seen in 17 cases in whom blood count was done. The lowest count of RBCs was 14 millions per cmm. of blood with 25 per cent haemoglobin. Out of 21 cases in whom leucocytic count was done, 13 cases showed normal counts. The remaining 8 cases had leucocytosis above 10,000/cmm of blood, the maximum being 27,500/cmm of blood in a boy admitted and treated as a case of bronchial asthma.

**Blood Kahn**—Out of 17 cases investigated, 2 cases had strongly positive, one had doubtful positive and the remaining negative result. In addition to 3 self-positive cases 2 other cases showed evidences of syphilis post-mortem. All these cases had syphilis as the associated disease and not as the primary disease affecting kidneys and leading to renal failure.

**Non-protein Nitrogen**—Non-protein nitrogen of blood is always raised in uraemia. Uraemia cannot exist in the presence of normal non-protein nitrogen, but the converse is not true, i.e., non-protein nitrogen may be much raised in the absence of true uraemia, e.g., in cases of pre-renal azotaemia. In all 56 cases investigated, it was raised considerably, the highest figure reaching 600 mgms per 100 cc of blood.

**Urea Nitrogen**—Out of 37 cases investigated, the highest figure reached was 300 mgms/100 cc of blood.

When renal failure sets in, urea and uric acid are retained in the body and are chiefly responsible for the rise of total NPN as shown below.

Total N P N	111 mgms /100 c.c of blood
Urea Nitrogen	88 mgms /100 c.c of blood

When total NPN is raised to a very high level, urea nitrogen forms about half of total NPN as shown in the following report.

Total N P N	600 mgms /100 c.c of blood
Urea Nitrogen	300 mgms /100 c.c of blood

It is important to note that very high level of N.P.N in blood does not always signify the greater severity of a case, particularly in those cases in whom vomiting and diarrhoea are marked. This is because in such cases, rise of N.P.N is due partly to renal factor and partly to pre-renal factor.

**Uric Acid**—When renal failure sets in, uric acid is the first to show the rise—even before the rise in urea occurs, whereas creatinine is the last to show the rise. Uric acid estimation was not carried out in any of the cases in this series.

**Creatinine**—The highest figure recorded out of 10 cases in which it was recorded was 10 mgms/100 c.c. of blood. When creatinine shows a definite rise above normal, it invariably means that the case is an advanced one.

**Cholesterol**—It was normal in all 14 cases in which it was estimated. When renal failure complicates nephrotic type of glomerulo-nephritis, blood cholesterol is usually high. In the present series 2 cases of uraemia were due to insufficiency setting in during the nephrotic phase, but cholesterol was not estimated in these 2 cases.

**Urine**—The onset of uraemia was preceded by a period of oliguria. The combination of oliguria and low specific gravity is very suggestive of uraemia. Urine was examined in 78 cases, but specific gravity was recorded in 16 cases only. In all these cases, specific gravity varied from 1010 to 1019. In addition, urine showed the presence of albumen, hyaline and granular casts, red blood cells and leucocytes.

**Cerebro-spinal Fluid**—Out of 19 cases examined, it was found to be normal excepting a little rise of protein and globulin in some cases particularly after an attack of convulsion. Urea and non-protein nitrogen contents of cerebro spinal fluid are raised in uraemia, but these were not estimated in any of the cases in the present series.

**Complications and Associated Diseases**—Cases of uraemia are very susceptible to complications, most important of which are pulmonary infections. Prognosis becomes very grave because they turn out to be terminal. Twenty-two cases had the following terminal complications.

Complications	No. of Cases.
Pneumonia or Broncho pneumonia	13
Pulmonary oedema	2
Empyema	1
Suppurative parotitis	2
Cellulitis of leg	2
Cancerum oris	1
Total	22

As regards associated diseases, most of them were detected on post-mortem examination held on 36 cases of uraemia and these are tabulated in post-mortem findings.

**Diagnosis**—Diagnosis is important from the point of view of giving prognosis. So varied are the clinical manifestations of uraemia



that unless one thinks of the possibility of uraemia, it is likely to be missed. Once the suspicion is raised, diagnosis can at once be confirmed by urine examination and estimation of non-protein nitrogen and urea nitrogen of blood.

**Prognosis**—It is always serious in true uraemia. Isolated cases might recover particularly those wherein the process that has produced the renal insufficiency, is susceptible of healing, e.g., renal failure during acute nephritis or in mercurial necrosis. Greater the nitrogen retention, worse is the prognosis, provided nitrogen retention is not due to pre-renal factor like vomiting and diarrhoea or in other words, larger the pre-renal factor in azotaemia, the better the outlook. Deepening of somnolence, convulsions, Cheyne Stokes breathing, marked oliguria, intractable hiccough etc., are symptoms of ill-omen. Complications like stomatitis, pericarditis, and pulmonary infections suggest that the end is near. The average duration of life after the onset of pericarditis, which occurred in 5 cases in the present series, was 7.6 days. Barach found average duration of life after pericarditis to be 29 days.

**Treatment**—**Diet**—All the unconscious patients were given milk diet and the rest were given lacto vegetarian diet. As regards the fluid intake, no definite data could be collected from the notes. Fluid intake was restricted in those cases complicated by congestive cardiac failure. Question often arises whether fluid should be given liberally or in restricted amount particularly when there is oedema or congestive cardiac failure. Fluid restriction will lead to more oliguria and azotaemia and the uraemic condition will get worse, whereas liberal intake of fluid will lead to more oedema. In this connection it is important to realise that oedema is any day a lesser evil than uraemia and treatment of impaired renal function should take precedence over that of oedema. With this view in mind, not only that the fluid intake was not restricted but glucose saline was given parenterally in 23 cases, 10 of whom had generalised anasarca. Other measures used to improve excretion by kidneys were saline, purine and mercurial diuretics, urea, thyroid extract, digitalis and intra-venous isotonic sodium sulphate (4.285 per cent). Dry cupping was done over the loins.

In order to promote extra renal excretion, the following measures were carried out: cathartics, electric bath, paracentesis abdominis or thoracis, and Southey's tubes.

**Venesection**—This has negligibly little detoxifying action in uraemia. It is useful in cases with cardiac failure occurring as a result of hypertension and may be life saving in acute cardiac failure due to sudden rise of blood pressure. Venesection was done in 15 cases in the present series.

**Symptomatic Treatment**—Sedatives—bromides, chloral hydrate, luminal paraldehyde and even morphia were used to allay the restlessness in some cases. Lumbar puncture was done in 22 cases for

diagnosis and as a therapeutic measure to reduce the severity of headache

*Blood Transfusion*—There is little danger in this procedure even in the presence of pronounced hypertension, if there is severe anaemia which needs blood transfusion. Blood transfusion was given to 2 patients in this series.

*Result*—Out of 98 cases, 95 cases expired and the remaining 3 cases were discharged against medical advice in a very serious condition.

*Autopsy Findings*—Autopsy was performed on 36 cases and the findings are given below.

Renal diseases in 36 autopsies	No. of Cases
Acute glomerulo nephritis	1
Subacute glomerulo nephritis	1
Chronic Gl Nephritis	15
Acute on top of chronic nephritis with pyaemia	
staphylococcal abscesses in kidneys	1
Nephrosclerosis	7
Pyelonephritis	2
Pyelonephritis with amyloid contracted kidney	1
Hydronephrosis due to a calculus	1
Hydronephrosis without any cause to account	1
Polycystic kidneys	2
Total No. of autopsies performed	36

Other autopsy findings are shown below and these show the complications and the associated diseases in 36 cases.

Post mortem findings	No. of cases
Pneumonia or Bronchopneumonia	8
Pulmonary Tuberculosis	6
Haemorrhages in the viscera	4
Renal calculi	4
Gall-stones	1
Hydrothorax	1
Syphilis	3
Visceral ulcers	2
Cancerum oris and empyema	1
Oedema of glottis	2
Haemorrhage in internal capsule	1
Salpingitis and hydrosalpinx	1
Atheroma of the aorta	3
Hypertrophied left ventricle	27
Total No. of autopsies	36

Out of 9 cases that showed haemorrhages in the viscera, 5 cases had in the stomach wall, 2 cases in the intestine, and 2 cases in the lungs. Syphilitic changes seen in 3 cases were most marked in the ascending aorta.

The idea of selecting the subject of uraemia is that uraemia has often been diagnosed wrongly i.e., it has been mistaken for many curable diseases and good prognosis had been given—on the other hand, diagnosis of uraemia is often made without any justification whatsoever, when it does not exist, and bad prognosis is given—both these are grave mistakes which can easily be averted by proper history, thorough clinical examination, and laboratory investigations viz., urine examination and non-protein nitrogen and urea nitrogen of blood, as discussed in the paper.



# THE INDIAN PHYSICIAN

*A MONTHLY JOURNAL OF CLINICAL MEDICINE*

**NATHOOBHAI D PATEL, M D ( Lond )**  
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*"There are men and classes of men that stand above the common herd, the soldier, the sailor, and the shepherd not infrequently, the artist rarely, rarer still, the clergyman, the physician almost as a rule He is the flower ( such as it is ) of our civilization, and when that stage of man is done with, and only to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race Generosity he has, such as is possible to those that practise an art, never to those who drive a trade, discretion, tested by a hundred secrets, tact, tried in a thousand embarrassments, and what are more important, herculean cheerfulness and courage, so that he brings air and cheer into the sick room, and often enough, though not so often as he wishes, brings healing "* —Robert Louis Stevenson

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# The Indian Physician

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*Let us remember*

## LUDWIG ASCHOFF

(1866—1942)

[Professor Ludwig Aschoff, the eminent pathologist whose name is associated with many outstanding contributions to physiology and pathology died on 24th June 1942. The following account is based on the obituary notices and tributes by his British students and colleagues.]

### LIFE SKETCH

"Ludwig Aschoff was born in Berlin on 10th January 1866, the son of a practising physician and is said to have determined on pathology as a career while a medical student. In this, he was influenced by his teacher, von Recklinghausen of Strassburg, with whom he served his first apprenticeship from 1891 to 1893, after qualifying at Bonn in 1889. From Strassburg, he passed on to Orth in Göttingen, where he remained for ten years, until his first call as a professor to Marburg at the age of 37 in 1903. His work there quickly established his reputation, and after only three years he was appointed professor of pathology in the pleasant university-town of Freiburg-im-Breisgau. Here he remained for the rest of his active life and in his retirement, resisting calls to Berlin and Vienna. All his life, he suffered from asthma, and this was his reason for remaining in the pure air of the Black Forest, which suited him well. Aschoff's long career in Freiburg, where he succeeded Ziegler, enabled him to build up a famous school of pathology, which attracted a succession of pupils from all over the world. He was a grand and unselfish chief, and much of the work which made him famous was done either in collaboration with his pupils or, if he was occupied with some other problem, under his direct inspiration.

"His first research work, carried out while a young assistant,

was on thrombosis and on appendicitis, and in both of these early problems he remained interested to the end. When he reached Marburg, two outstanding pieces of work soon appeared—with Tawara on the atrio-ventricular node of the heart (Aschoff-Tawara node) and his own work on the morbid anatomy of acute rheumatism ('Aschoff bodies' in the myocardium and lungs). Here, too, he began, with Adam—his first pupil from the British Empire, the investigation of the significance and pathology of doubly refracting fats, work which continued along many different lines and for many years at Freiburg in association with his pupils, among whom Kawamura (atherosclerosis), Bacmeister (gall-stones and gall-bladder pathology) and Landau (suprarenal cortex) may be mentioned.

"Next came the developments of vital staining, which Ehrlich's work on dyes had made possible, and the researches of many pupils finally culminated in Aschoff's generalisation of the reticuloendothelial system. The functions and pathology of this system kept Aschoff and his pupils at work for years, and the conception of this system of cells will always be associated with his name. Work was also done on tuberculosis, on gastric ulcer and again on his old problem of appendicitis. During the war of 1914-18, he played a prominent part as a pathologist in the field, and his work on scurvy and gas-gangrene at this time is well known."

During his professorship at Freiburg, he had, as his colleagues many distinguished workers in other branches of medical science. He retired from his chair at the end of academic year 1935-36. Aschoff's 70th birth day was celebrated with great pomp in 1936 and messages of congratulation were received from all over the world.

#### CONTRIBUTIONS TO MEDICAL HISTORY

But even after retirement in 1936 and at the advanced age of 70, he was not idle or resting on his past work. In pathology, he continued his activities by his study and investigations of the changes associated with old age. Besides, he utilised his leisure and mature years to develop to the full his love for the history of medicine. The top floor of the institute was given over to the department of the history of medicine and he became its first director. The fruits of his medico-historical studies were given to the public in his Finlayson lecture in Glasgow in 1938 and his last published book, a brilliant history of pathology is

the *proto-plasma* monograph (1938) He was also working on the early history of syphilis.

#### THE MAN AND HIS LABORATORY

He was a small wiry man with dark hair standing up and was lively and energetic to an intense degree The laboratory was rather poorly equipped It had various rooms, some small and some large and no one had more than a very short bench space. There were only two laboratory assistants, one for the post-mortem room and one chiefly to look after experimental animals About 1912, "his busy day began in the institute at 8 a.m. when he demonstrated the morbid anatomy of recent post-mortem examinations to his assistants and post-graduate students, and also talked of many other things He made use not only of post-mortem material obtained in his own institute on the previous day, but also that produced from evil-smelling metal boxes which came by rail from prosecutors in neighbouring towns without a medical school, e.g., Karlsruhe Chaff and discussion were very free at these early morning meetings, and bits of tissue were doled out for histology to various pupils interested in particular organs and problems Sometimes, the material was fresh and good for histology, often it was not so good' Later in the morning there was a fixed time at which pupils could show their sections to Aschoff and discuss their work, and after that came the morning lecture to the huge undergraduate class Aschoff's assistants and post-graduate pupils all attended, sitting in the front rows, and the Chief often managed to slip in a reference to recent work by one of the pupils present, which the class always hailed with great delight" Work continued during the week till 6 or 7 p.m. but on Saturdays and Sundays the laboratory was almost deserted Even in 1936, the daily routine of the Institute was the same starting at 8 a.m. "But in addition to his demonstrations of post-mortem and surgical material Aschoff would review the journals and books which were going into the Institute Library The rest of the day was taken up with attendance at the students' lectures, individual work and pauses for refreshment Not the least important of these was the 4 o'clock break for tea or coffee (Aschoff had introduced this when he came back from London after working in the Hospital for Tropical Diseases in the early part of the century) which the Chief usually attended, and often regaled us with stories of his experiences in his world travels."

## LIGHTER SIDE OF HIS LIFE

At the week end, Aschoff took an active part in all the relaxation and fun and joined laboratory parties, sking in winter and making excursions on foot in summer. In the evening he loved to join a circle where beer and wine circulated freely. "His enthusiasm for his studies also took him outside the laboratory. There was a great day when it was rumoured that a dog with a goitre had been seen at Glottertal and the whole Institute, led by Aschoff, went off to investigate the matter, the dog was not found but we consoled ourselves with a libation to Hoselips, the local Bacchus. On another occasion, there was a fair at Freiburg with a dwarf circus, and we were exhorted in the students' lecture to visit it to study the achondroplasiacs, the cretins and the Lorraine dwarfs." He was also much interested in duelling. "The class in those days was an odd one to look at. There were of course both men and women, and always a number of male students with their heads bandaged and faces covered with plaster from the duelling which was then in fullest swing. This sport was strongly approved of by Aschoff, who himself, like many of his German assistants and pupils, had ample scars to show. He made arrangements for us to see the duelling (Mensur) which took place in an inn just outside the boundary of the town."

## ASCHOFF AS A TEACHER

Aschoff's pupils themselves say that Professor Kettle's description of Aschoff cannot be bettered. "To hear Aschoff lecture, to see that frail form quivering with the eagerness of exposition, is an experience never to be forgotten. One is reminded of a racing speed boat, throbbing with the power that shakes the whole craft into impetuous motion." "The clarity and succinctness of his analyses were extraordinary. It mattered not whether it was recent paper on endocrinal interplay, the atmospheric conditions in the stratosphere or some advance in the pathology of viruses, it would be explained simply and precisely and if an assistant was working on the problem he would be given the book to read. It always amazed us where Aschoff found the time to read so much, for the journals taken by the Institute were numerous, and while working there, one realised the enormous advantage of having extensive departmental libraries in addition to the central University library."

## ASCHOFF'S MENTAL QUALITIES

"One need not speak of Aschoff's ability in the ordinary sense—it was of a rare order, but one may emphasise the width of his knowledge, his keen interest in other branches of science, and, above all, his quite unusual alertness of mind. In investigating any condition of disease the question for him was not merely what the structural changes were but also how they had been brought about, and in answering the latter he recognised that other methods than those of pathological anatomy were required. A good example of this is afforded by his investigations on gall-stones. His work accordingly came to be characterised by breadth of outlook and freshness of treatment. His knowledge, both in extent and in detail, of what had been done by others was remarkable, his activity in observation was keen and unceasing and he seemed to have the faculty of remembering everything he saw or heard, a faculty which was retained in striking degree even in his later years. The result was that he possessed a storehouse of pathological knowledge, one may say of erudition, almost unequalled, and one which he always held in full command. And equally remarkable was the use he made of this storehouse of knowledge. By thinking and questioning, he was ever engaged in co-ordinating facts and establishing principles. This is well exemplified in the case of the reticulo-endothelial system. Many of the facts with regard to it, as a strong and defensive mechanism, were already known, but there were necessary an insight and comprehensive grasp such as he possessed to make a coherent whole and to establish the real importance of the system in both normal and abnormal states. In contrast to this power of generalising was his liking for analysis and classification. This is a feature in his *Lehrbuch*, indeed, it seems to me to be sometimes carried even to excess, it is apparently the outcome of his philosophical bent, in any case, it is to be considered in an estimate of his mental qualities. These are some of the thoughts which come to me in viewing Aschoff's work as a whole, but his publications will be his true and faithful monument. Regarding Aschoff's position in the world of pathology there can be but one opinion—he was pre-eminent in his day. Since Virchow's time, I know of no one whose work has led to such important advances in so many fields." One cannot help echoing the feeling and regrets of Professor Robert Muir "Truly, a rare spirit has gone from us"

—D V S.

# Original Contributions

## PENICILLIN

### A SHORT NOTE

By

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Penicillin, a bacteriostatic and bacteriocidal substance of unknown composition, is the active principle of the mould *Penicillium notatum*. There are many varieties of the mould but only *notatum* gives rise to this substance. Prof Fleming was the first to note the bacteriostatic property of this mould in 1929. He observed that the contamination of plate cultures by this mould prevented the growth of other organisms in the surrounding area. He also found that the liquid medium in which the mould was grown, when freed from the mould itself, had the same property of preventing the growth of certain organisms. He then tested this substance on leucocytes and found that they were unaffected by it. The work on penicillin was in abeyance for some time after its discovery until Prof Florey revived the subject recently (1941). Since then a large amount of work has been done on it with a view to utilise the bacteriostatic property of the mould for therapeutic purposes.

Penicillin is effective against the gram positive organisms in general and only the gonococcus and the meningococcus of the gram negative organisms are sensitive to it. The great advantage of penicillin over the other bacteriostatic substances is its harmlessness. It can be given in very large doses without fear of any toxic effects. It is effective in very high dilutions. Pure penicillin would inhibit the growth of the sensitive organisms in a dilution of 1 50,000,000 to 1 100,000,000. It acts also in the presence of pus, blood, serum, and tissue autolysates. In contrast to the above advantages there are certain drawbacks.

The amount of penicillin produced by the mould *P. notatum* is extremely small and the substance is very unstable in its crude form. It is destroyed by boiling, by oxidizing agents, such as hydrogen peroxide, by the enzymes produced by certain bacteria and contact with heavy metal ions like copper. It is

affected also by acids and alkalies. The sodium and calcium compounds retain their activity for about 35 days while the barium compounds retain it for about 8 months. In addition to the extremely small yield of the penicillin it requires about a week for its production by the mould.

Penicillin is produced by the mould during the period of its growth. The medium generally used is a liquid one, usually some modification of Czapek Dox's medium. The mould grows freely on the surface of the medium and in about 10 days forms a greenish blue growth, which covers up the entire surface of the medium. 24°C is a suitable temperature for its growth. At lower temperature the growth is delayed. It does not grow at 37°C. The mould is allowed to grow for 10 days when the yield of penicillin is maximum. At this stage the medium, now containing the penicillin, is drawn off from under the mycelium and is replaced with fresh medium in which more penicillin will form in about half the time required for initial production. The medium can be changed several times in this way. This crude extract has usually an activity of 1 to 2 units per cc. The crude substance is purified and concentrated. The dried and purified therapeutic penicillin has an activity of 40 to 50 units per mg.

For some time past I have been growing this mould, *Penicillium notatum*, on wheat bran medium for production of penicillin. This medium was first used by S. Srinivasrao of Bangalore. The wheat bran is moistened with water, put up in flasks and autoclaved. It is then inoculated with a spore suspension of the mould. The cultures are kept at room temperature and each flask is shaken thoroughly twice a day. The colour of the medium after autoclaving is brown. 24 hours after the inoculation with the mould the colour of the medium becomes whitish and hazy. 48 hours after the inoculation the colour changes to a light green and in 72 hours it becomes dark green. The cultures become green when the spore formation is abundant. At this stage penicillin is extracted from the medium by using distilled water. The resulting product is a slimy green liquid. This is filtered through filter papers and a liquid with a colour ranging between pale reddish yellow to deep port wine is obtained. This is the crude extract. This extract is now sterilized by passing it through L1 and L3 candles. The crude extract thus obtained contains a bacteriostatic substance and as it is obtained during the growth of the mould *P. notatum*, it may be



taken as penicillin. It is possible that this crude extract may contain bacteriostatic substances other than penicillin. The activity of penicillin in this crude extract is about 24 to 32 units per c.c. This extract is very unstable and even when kept at low temperature, there is a considerable loss of its activity within a few days.

There are various ways of estimating the activity of the penicillin, e.g. the Gutter or the imprgnated strip method, the hole or the Agar cup method, Prof. Florey's glass cylinder method and the titration method. I am using the last method as it gives very accurate results. The test organism used is the staphylococcus aureus and the medium used for estimating the activity is the one recommended by Prof. Fleming. The medium consists of glucose, peptone, sodium chloride and Andrade's indicator. Staphylococcus growing in this medium ferments the glucose and produces acid which changes the colour of the medium to red as the medium contains Andrade's indicator. Staphylococcus aureus is used as the test organism as it is very sensitive to the action of penicillin.

Serial dilutions of the crude penicillin are made in this medium ranging from 1/50 to 1/6400. These dilutions are put up in small test tubes in 2 c.c. quantities each. A drop of saline suspension of the test organism, the staphylococcus aureus, prepared from a 24 hours Agar culture and adjusted to match in opacity to the No. 2 tube of Brown's Opacity standards tubes, is now added to each dilution of the series. The staphylococcus suspension is matched against a definite opacity tube in order to get a uniform inoculum of the test organism in all the titrations for the activity. A tube which contains a highest dilution of penicillin and yet has not allowed the test organism to grow as determined by the absence of red colour in the medium is looked out. This tube indicates the activity of the penicillin which is expressed in terms of units per c.c. A tube which shows any slightest red colour indicates that the test organism has grown in it and the penicillin dilution is ineffective to check its growth. The crude extract as prepared above has an activity of 24-32 units per c.c. as stated before.

Purified penicillin can be used locally as well as intravenously. It is supposed to be not effective when given by mouth as the acidity of the gastric contents is likely to inactivate it. Cases have been reported, however, where oral administration

of penicillin has given promising results. Penicillin produced by me on wheat bran medium has been used in a few cases. It was mainly employed in the form of local applications only. Two cases of burns were not responding to any treatment including sulphonamide group of drugs. With the combined local and oral use of penicillin these cases responded extremely well. Two other cases of burns, which were being treated with local treatment only also gave very good results. A case of very chronic ulcers, not responding to any form of treatment including sulphonamides has given good results with local use of penicillin. A case of lung abscess and a case of suspected unresolved pneumonia were treated by giving the penicillin by the oral route. About 10 grains of soda bicarbonate were given by mouth to the patient 5 minutes before the oral administration of penicillin with a view to raise the pH of the gastric contents. No improvement in the local condition was noted in these cases though there was some lowering of the temperature. The doses were absolutely inadequate as only 6,000 to 8,000 units were available per day whereas at least a hundred thousand units were indicated per day in these cases. In addition to the extremely small doses, penicillin was given by the doubtful oral route as the crude extract was not in a suitable state for parenteral use. In addition to oral route of giving penicillin in these cases instillation of the drug directly into the larynx in small amounts was tried with the idea that it may reach the lesions in the lungs directly. A case of sinusitis with chronic nasal obstruction which failed to respond to any treatment including autovaccine has shown satisfactory response to the local use of penicillin. A few other cases are treated with good results. A report on all these cases will be given in detail in a paper to be communicated later. In one or two cases which have been treated upto now it seems that penicillin has been effective in controlling the local sepsis as well as lowering the temperature even when it was given by the oral route only.

Two rather interesting facts were observed during the course of the growth of the mould. One was the great increase in the pigment production by the mould, so that the crude penicillin had a port wine colour instead of the usual reddish yellow. This increased production of pigment was especially noticeable on repeated subcultures of the mould. The other interesting fact was that in a batch of culture flasks, in which each flask was

identical with the other as regards the amount of medium, the moisture, the time and the size of the inoculum, etc., one or two flasks failed to develop the green colour at the end of 72 hours while the rest developed it as usual. This phenomenon was invariably observed with each and every batch of flasks, one or two flasks from every batch failing invariably to develop the green colour.

The work on penicillin is being continued further with a view to reduce the time of production, and to increase the yield of penicillin and attempts are also being made to purify and concentrate the crude extract.

*P.S.*—The case of lung abscess referred to above has now turned out to be a case of tubercular affection of the lung which would explain the failure of the penicillin treatment. After this article was written, it has been possible to concentrate the crude extract and even to produce it in a partially dried form, though methods are still in an experimental stage.

(A paper read before the Meeting of Teaching Pathologists of Bombay on 26-2-1944.)

## DIAGNOSIS OF EPILEPSY BY MEANS OF METRAZOL

Roismiser (*Semana Medica*, Buenos Aires, Feb 11, 1943, 50 310), points out that metrazol shock therapy led to the use of this substance in the differential diagnosis of epilepsy. He described his observations on 56 subjects, 38 of whom were epileptic and 18 were not. Of the first group 92.1 per cent responded with a typical crisis to the intravenous injection of 3 cc or less of a 10 per cent solution of pentamethylenetetrazol. The test was always begun with the injection of 1 cc. Two of the epileptic patients reacted with an attack to this dose, 3 reacted to 1.5 cc, 12 to 2 cc, 8 to 2.25 cc, 2 to 2.5 cc, 8 to 3 cc and 3 required more than 3 cc for the production of a crisis. The 18 subjects who were not epileptic all required more than 3 cc for the production of a convulsive attack. (*J Am Med. Assoc* July 24, 1943, 122 903)

# SERUM PHOSPHATASE IN MALIGNANT TUMOURS

*By*

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Many tissues contain enzymes which are capable of hydrolysing the organic phosphorus compounds and liberating free phosphoric acid. These enzymes are known as phosphatases. One type of these enzymes is present in the osteoblasts, the hypertrophic cartilage cells and certain cells of the periosteum. It hydrolyses salts of phosphoric esters brought to the ossifying zone by the blood and causes a local increase in phosphate ions. A deposition of calcium phosphate results in the vicinity of the cells during bone formation (Robison, 1923). Some of these enzymes are active in an alkaline medium and others in an acid medium. The phosphatase of bone (Yamane, 1931), bile (King and Armstrong, 1934) and white blood cells (Roche, 1931) are alkaline phosphatases, while those of liver (Bauman and Riedel, 1934) prostate (Gutman and Gutman, 1938) and red blood cells (Roche and Latreille, 1934) are acid phosphatases. Woodard and Craver in 1940 found that the normal lymph nodes, Hodgkin's nodes and lymphosarcoma tissue contain both acid and alkaline phosphatases. Kabat and Furth (1941) have carried out histochemical investigations on alkaline phosphatase content of various normal and neoplastic tissue, by the technique described by Takamatsu and by Gomori. They have shown that alkaline phosphatase activity is a characteristic of certain cells. Among normal cells the epithelium of the small intestine, the proximal convoluted tubules of the kidney, the osteoblasts and the endothelium are particularly rich in phosphatase. Acid and alkaline phosphatases are also normally present in the blood serum. The major portion of alkaline phosphatase is obtained from bone. Of the tumours which have been studied the phosphatase is present in malignant osteoblasts of a transmissible chicken sarcoma and in an osteogenic tumour of the mouse. In non-bone forming strains of transmissible chicken sarcoma, the enzyme is absent. The enzyme is also absent in carcinoma of the breast.

There are two methods generally employed for the determi-

nation of alkaline phosphatase in blood and other tissues. One is known as the Kay's method and the other is that of Bodansky. The unit of phosphatase according to Kay is defined as the amount of phosphatase in one cc of serum that will liberate one mg of phosphorus from sodium  $\beta$ -glycerophosphate at a pH of 7.6 in forty-eight hours at a temperature of 38° C. According to this method serum from a normal adult contains 0.10 to 0.21 of a unit, while children have a higher value, 0.17 to 0.34 unit. The method of Bodansky is more widely used and according to that method, a unit is the amount of phosphatase in 100 cc of serum that will liberate one mg of phosphorus from sodium  $\beta$ -glycerophosphate at a pH of 8.9 in one hour at 37°C when no more than 10% of the substrate has been used up. The values obtained by Bodansky's method are higher than those of Kay, in the normal adult being 1.5 to 4 units and in growing children 3.1 to 13.1 units.

As regards the acid phosphatase activity, it is determined by a similar method as outlined above except for the change in pH of the buffer solution, since the acid phosphatases act at pH=5. The range of values for acid phosphatase in blood in normal subjects is 0.5 to 2.5 units (Gutman A. B. and Gutman E. B., 1938).

The determinations of alkaline and acid phosphatase in blood are many times of diagnostic importance in disease.

#### ALKALINE PHOSPHATASE

Kay in 1929 and Roberts in 1930 reported the quantitative phosphatase determinations on the blood of patients with diseases of bone. Subsequently this procedure was introduced into the clinical studies of bone lesions. The findings by Gutman and Gutman (1938), Williams and Watson (1941) and by others showed that, except in cases with jaundice, the serum alkaline phosphatase is increased whenever there is a tendency for the body to form new bone or an attempt to do so. Thus it is high in normal children because the bone is growing. It is very high in rickets because the bones are attempting to grow but are prevented from doing so because of some factor or factors which are responsible for the faulty calcium or phosphorus metabolism in that disease. It is high in hyperparathyroidism and the excess production of phosphatase probably indicates the defence reaction on the part of bones against the osteolytic process which is stimulated by parathyroid hormone. It is high in Paget's disease of bone and also in cases with primary or

metastatic bone tumours When cancer originating in a soft part metastasizes to bone, phosphatase is probably produced not by the invading tumour but as a part of a defence or healing reaction in the adjacent bone

#### ACID PHOSPHATASE

Kutscher and Wolbergs (1935) found that normal prostate tissue is extraordinarily rich in acid phosphatase This observation was confirmed for normal and carcinomatous prostate tissue by Gutman, Sproul and Gutman (1936) Gutman and Gutman (1938) found significantly increased acid phosphatase activity of serum in 11 out of 15 patients with metastasizing prostate carcinoma

At the Tata Memorial Hospital which is primarily devoted to the treatment of cancer and allied diseases, the determination of acid and alkaline phosphatase in blood is carried out in the biochemical section, as a routine investigation, in cases of tumours clinically suspected to have originated in bone or in prostate During a study of about 27 cases, that were admitted in this hospital during the first  $1\frac{1}{2}$  years since the beginning of the hospital, Chitre (1943) found variable rise in alkaline blood phosphatase In some cases of osteogenic sarcoma, the phosphatase value was found to be high but in some there was no rise even though the radiological examination showed considerable new bone formation This finding was in agreement with that of Woodard and Higinbotham (1941) who also could not find definite correlation between the level of serum phosphatase and its concentration in the tumour tissue According to Franseen and others, the product of the volume of the tissue and its phosphatase concentration was taken The values thus obtained could not be correlated to the level of serum phosphatase It was therefore suggested by Chitre that the level of serum phosphatase in bone tumours is determined by some factor or factors which are not yet clearly understood, and that this variable behaviour could be possibly explained by an enhanced excretion of the enzyme in some cases It is therefore intended to undertake a planned investigation to elucidate this problem a little more clearly

In the meanwhile it may be interesting to cite as an example the notes of two cases which illustrate the assistance that may be derived by determination of serum phosphatase in arriving at a clinical diagnosis

## DETERMINATION OF ACID PHOSPHATASE

An old man of 53 (†5230) with the complaint of having increasing difficulty in micturition for the last three years was admitted in this hospital on 9-9-1943. He was suspected to be suffering from a carcinoma of the prostate. An aspiration biopsy on 14-9-1943 was reported as not being adequate for a pathological diagnosis on the basis of an examination of the smears. In the meanwhile the patient's blood was examined on 13-9-1943 for the acid phosphatase content. The acid phosphatase value of the serum was 5.6 units which was high enough to warrant a diagnosis of prostatic tumour. The patient was operated on 13-10-1943 and the operated tissue was examined histologically. The pathology report was hyperplasia of the prostate with definite precancerous changes. This case showed the importance of acid phosphatase determination in judging the malignancy of prostate even in its precancerous condition.

## DETERMINATION OF ALKALINE PHOSPHATASE

A case was demonstrated by Dr K. G. Munsiff at one of the clinical conferences on 21-1-1944 (see, *The Indian Physician*, Feb, 1944, pp 48-9). The patient was a man of 55, with an ovoid soft swelling above and parallel to the middle third of the clavicle. The swelling was of two months' duration and accompanied by pain. An x-ray picture showed a slight rarefaction of the right clavicle just under the swelling. A thorough search had revealed no primary neoplastic condition in any other part of the body. A piece of tissue from the tumour was removed for biopsy. The histological examination was suggestive either of an epidermoid carcinoma or an adamantinoma. Serum phosphatase determination gave the results—acid phosphatase 2.1 units and alkaline phosphatase 19.6 B.U. The clinicians as well as the pathologists have not yet made up their minds finally as to the nature of the lesion and it is hoped that high alkaline phosphatase value would help them to arrive at a definite conclusion.

The determination of serum phosphatase has helped the clinicians as well as the pathologists in many similar cases at this hospital. It was carried out in 84 cases of tumours suspected to be arising from the bone and prostate as well as those suspected to have caused metastasis in bones. The total determinations were 107. The value of such determinations as an aid to clinical diagnosis is summarised in the following table.

TABLE  
TOTAL DETERMINATIONS 107 ON 84 PATIENTS

Determination in	Osteogenic Sarcoma	Giant Cell Tumours	Ewing's Tumours	Prostate Tumours	Bone Metastasis	Lesions in which Bone origin was suspected
No. of cases in which the determination supplemented the clinical and histological findings	7	0	10	1	14	22
No. of cases where it did not give any useful information	5		2	1	6	4
Total	12	0	12	2	20	26

In 3 cases no diagnosis could be established

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# Society Proceedings

The 34th Meeting of the Seth G S Medical College and K E M Hospital Staff Society was held on Saturday the 12th February, 1944 at 9 p.m. (S.T.) in the Main Lecture Theatre of the College. Dr Abdul Hamid was in the chair, and Dr N K Sahlar read a paper on

## SOME OBSERVATIONS ON TETANUS

The object of my paper is to take stock of tetanus cases admitted in the K E M Hospital from 1st August, 1941, since when all cases of tetanus were admitted in my sole charge. Between 1st August 1941 and 31st July, 1943, 319 cases were admitted under me, and in this paper I shall only deal with these 319 cases. Though I had treated, at the K E M and G T Hospitals, tetanus cases prior to August 1941, on the same lines, I have excluded them from this paper for one reason or another.

Table No. I. Cases from August 1939 to July 1943

Year	Aug 1939 to July 1940	Aug 1940 to July 1941	Aug 1941 to July 1942	Aug 1942 to July 1943
Total No. of cases	130	113	146	173

Table I shows the number of tetanus cases admitted yearly at K E M Hospital from August 1939 to July 1943. Out of these cases I am solely responsible for 319 cases only. Some of these cases were admitted and died within a few hours of admission. They were moribund and neglected cases, so bad that nothing could have saved them. To judge fairly the results of treatment adopted in this series, I have attempted to show separately all cases that died within twenty-four hours of admission and those that survived the first twenty-four hours.

Table No. II. Mortality Rate

Cured	167 (52.5%)
Otherwise	4 (1.2%)
Died within 24 hours	46 (14.4%)
Died after 24 hours	102 (31.9%)
Total	319 cases.

Table II shows 319 cases admitted in two years at the K E M Hospital. Out of these, 167 cases (52.5 p.c.) were completely cured. 4 cases were discharged against medical advice, 148 cases died. Out of these 148 cases, 46 (14.4 p.c.) died within the first twenty-four hours. If we exclude these cases, then out of the total of 319 cases, 102 cases (31.9 per cent) died after 24 hours. This leaves us with the mortality rate of 31.9 per cent in my series of cases between August 1941 and July 1943.

Table III Age Group

Age	1-10 yrs.	11-20 yrs	21-30 yrs	31-40 yrs	41 upwards.
Cured	61 (56.1%)	34 (34.2%)	42 (58%)	14 (35%)	16 (88%)
Unknown	4 (3.6%)				
Died within 24 hrs	20 (18.0%)	8 (15.1%)	9 (12%)	3 (7.5%)	6 (14.2%)
Died after 24 hrs	24 (22.0%)	11 (20.7%)	24 (32%)	23 (57.5%)	20 (47.8%)
Total	109	53	75	40	42

*Age* Out of these 319 cases treated 109 cases were under ten years of age. This is a high rate of tetanus in children, but it is simply due to the vicinity of one of the largest children's hospitals from where cases are transferred here. In Table III we see the total number of cases at different ages and death rate at different periods of life. From this series we find that the highest mortality rate is after 30 years. Though it is generally believed that tetanus in children and the aged has a high mortality, in our series children only show a mortality rate of 22 per cent whilst cases aged 30 years and over show a high mortality rate.

Table IV Incubation Period

Days	1-5	6-10	10-upwards	Unknown
Cured	29 (40.8%)	38 (49.5%)	49 (65.4%)	51 (53.2%)
Unknown		1 (1.3%)		3 (3.1%)
Died within 24 hours	15 (21%)	8 (10.3%)	5 (6.5%)	18 (18.7%)
Died after 24 hours	27 (38.2%)	30 (38.9%)	21 (28%)	24 (25%)
Total	71	77	75	86

The incubation period is the period in days between receiving the injury and the manifestation of the first symptoms of the disease. In this series it is seen that when the incubation period is short i.e. 1-5 days, the total death rate is high e.g. 59.2 per cent. On the other hand when the incubation period is 10 days and upwards the death rate is 34.6 per cent. This is in keeping with the observations of various observers on this subject. An incubation period of less than five days indicates a fatal issue and one of more than ten days a good prognosis, but an incubation period between five and ten days gives no indication as regards the prognosis.

Table V Duration of disease before giving treatment

No. of days	1	2	3	4	5	6-10	11 above	Unknown
Cured	24 (30.6%)	49 (50%)	32 (64%)	25 (31.2%)	6 (7.5%)	21 (26.2%)	5 (6.2%)	5 (6.2%)
Unknown	3 (3.7%)							1 (1.2%)
Died within 24 hours	16 (20.2%)	15 (15.3%)	5 (10%)	3 (3.7%)	1 (1.2%)	2 (2.5%)		4 (5%)
Died after 24 hours	36 (45.5%)	34 (34.7%)	13 (26%)	13 (16.2%)	1 (1.2%)	3 (3.7%)	1 (1.2%)	1 (1.2%)
Total	79	98	50	41	8	26	6	

*Duration of disease before giving treatment* —All cases admitted in the ward with the diagnosis of tetanus required serum treatment at once. But this does not mean that all received serum as soon as the malady began. Some seek hospital treatment late after the onset of the malady whilst others are admitted immediately. In our series we observe that those cases who required serum one day after the onset of the malady show a high mortality rate (65.7 per cent). On the other hand those who received serum five days after the onset of the malady show a mortality rate of 25 per cent only. When the cases admitted in the wards show a long duration of the disease, it is generally observed that they are mild and recover quickly, whilst those with very short duration of the malady are toxic and stormy cases. From this we can safely conclude that the mortality rate is in inverse proportion of the duration of the disease.

Table VI Complications

Type of complications		Died	Cured
1	Lung complications (a) Pulmonary oedema (14)	2	32
	(b) Pneumonia (5)	2	3
2	Serum complications (20) (a) Anaphylactic shock (3)	2	1
	(b) Arthritis (3)	3	
	(c) Rash (14)	11	
3	Hyperpyrexia (2)	0	2
4	Parotitis (1)	0	1
4	Thrombosis of Brachial vein (1)	1	
6	Facial Palsy (1)	1	
Total		25	39

Out of 319 cases of our series 64 cases (24.06%) showed complications. Of these 64 cases, 39 were lung complications, 20 cases showed serum complications, two had hyperpyrexia, one parotitis, one thrombosis. Out of these 64 cases with complications, 39 cases (62.25 per cent) died. This bears out the fact that any complication in tetanus is a very bad accompaniment.

From Table VI one can see that out of 39 cases that died of complications, 35 cases died of chest complications (32 oedema of the lung and 3 of pneumonia). The one case that died of anaphylactic shock was the solitary case of fatal anaphylaxis in our series of 319 cases. From this table it is clearly seen that chest complications and particularly oedema of the lungs are the most dreadful complications we have encountered in our series.

*Site of Injury* —Our cases were classified according to the site of injury as follows —(1) Head and neck, 77 cases, (2) Trunk, 21, (3) Upper limb, 32, (4) Lower limb 135 and (5) Unclassified 54.

Table VII Site of Injury

Site.	Head and neck	Trunk	Upper limb	Lower limb	Unclassified
Cured	48 (62.4%)	2 (20%)	20 (62.5%)	70 (52%)	20 (63.8%)
Died	29 (37.6%)	17 (80%)	12 (37.5%)	65 (48%)	25 (40.2%)
Total	77	21	32	135	54

Referring to Table VII the first thing that strikes us is the highest death rate (80 per cent) when the site of injury is the 'trunk.' Out of these 17 cases that died (a) 8 cases were of uterine origin, four

pneuperal sepsis and four of abortions, with a stick in the uterus in one of them, (b) 3 cases were of umbilical origin with the involvement of the umbilical cord in one of them, (c) one case of sacral bed sore, (d) one of scrotal operation, (e) one of perineal injury, and (f) one of anal injury. In this series all cases of uterine or vaginal origin died inspite of local treatment and the active co-operation of the gynaecological department. So any site of entry of tetanus round about perineum bears a very bad prognosis. The next in series is 'lower limb' (48 per cent). Out of 135 cases admitted with injury to lower limb, 104 cases were below the knee (feet 99, heel 1, toes 3, ankle 1). Out of these 99 cases of feet injury 44 died (44.4 per cent). Out of 77 cases of Head and Neck injury, 44 were cases of discharge from ears, 22 injury on head, 9 injury on face, one operation on eye, one injury on neck. The majority of these cases had discharge from the ears. But to label the 'ear' as the portal of entry is rather doubtful because many children admitted as tetanus had ear discharge though they had definite extra-aural sites of entry of tetanus bacilli, and aural discharge is a very common manifestation in the out-door department of any children's hospital.

In this series 'upper limb' shows the lowest mortality. Out of 32 cases—24 cases were examples of injury to hand (including fingers), and out of these 24 cases 8 died (33.3 per cent).

So in conclusion, in our series of 319 cases the 'trunk' site shows the highest mortality, the next is lower extremity, and the lowest mortality is in the groups of head and neck and upper limb.

*Types of Injury* —The type of injury received in our 319 cases were various. I have tried to classify them as follows —

- (a) Operations —Abdominal, amputation finger, removal of eye ball, piles, scraping osteomyelitis, amputation etc
- (b) Genito-Urinary —Abortions, puerperal sepsis, scar after operation
- (c) Injuries —(i) cuts from glass, lion, nail, stones, tin, thorn  
(ii) Quinine injections, rat-bite, dog-bite, fractures, branding, burns, vaccination, guinea worm ulcers, scabies, gangrene of limbs, kick on buttock

### *Treatment*

The treatment of active tetanus can be divided into three parts —  
1 Treatment of wounds 2 Specific antitoxin 3 General treatment including treatment of spasm, rest to the patient and feeding

1 *Treatment of local wound* —We do not touch the local wound before giving antitoxin, and then also we touch it very little. Scabs and foreign bodies are removed and the wound is freely irrigated with  $H_2O_2$  and is dressed with light bandage or better still with porous gauze. Care is taken to see that superficial healing does not take place.

2 *Specific anti-toxin* —The chief treatment of tetanus is the administration of antitoxin to neutralise the toxins. The antitoxin used in this series of cases, was supplied by the Haffkine Institute and throughout these two years no other brand was ever used in my ward. The idea of giving anti-toxin is to neutralise the toxin. But where

is the toxin present? In the first place the toxin is present in the wound, and tries to reach the central nervous system from the local site and fix itself in the motor cells of the central nervous system. Some toxin from the local site passes up the axis cylinders of motor nerves, some traverses the axis cylinders and become fixed to motor nerve cells and some diffuses in the central nervous system.

*Route of giving antitoxin* —In these circumstances, the route of giving the antitoxin is of great importance. The antitoxin, administered by whatever route, must reach and neutralise the toxin in the shortest possible time. There are three routes for giving the serum, (a) Intravenous, (b) Intramuscular, and (c) Thecal administration. In our series of 319 cases we used only intravenous or intramuscular route or both combined. In children we gave serum in the muscle and in adults we gave either in the vein or in the muscle or used both routes in combination. In not a single case out of 319 cases we had recourse to spinal route of administering the serum. In these two years we had done lumbar puncture only three times and that too, to diagnose infective meningitic cases, wrongly diagnosed as tetanus and admitted in my ward. Long before the observation of these cases, I used to treat cases of tetanus at the G. T. Hospital for some years. There I freely used the spinal route for administration of serum. Intravenous and intramuscular routes were also used. But for some time my first dose was in the theca. By experience I soon found out that cases with sera in the spine did not fare in anyway better than those in whom sera were given in the vein or muscle. On the other hand, I realised that repeated cysternal or lumbar punctures with the help of anaesthesia produced chest complications, like oedema of the lungs and pneumonia. Also administration of serum in the theca, led to sterile meningitis. So with this clinical experience, when I began to deal with the present series of cases, the route of administration of serum was either intramuscular or intravenous or in some cases both combined.

Besides this clinical observation, we have reasons to believe that all parts of the central nervous system including the spinal cord are richly supplied with blood vessels and capillaries and any antitoxin given intravenously would reach the central nervous system more quickly than by the thecal route.

*Dose of anti-toxin* —The dose we gave to our patients was rather high and we aimed at giving the maximum dosage in the minimum time. We generally gave 250,000 units within twenty-four hours of admission. We were supplied with concentrated sera (20,000 units in 7 cc). Our first dose in adult patient was 120,000 units and the same dose was repeated within twenty-four hours. The route preferred was venous one. We had enough justification to continue with these two doses treatment of tetanus for a very long time viz 18 months. Then in the latter part of the second year, our patients began to show anaphylactic reactions and shock, pyrexia and hyperpyrexia, immediate oedema of the lungs and many showed, a few days after administration of serum chest complications. So we reduced our first dose from 120,000 units to 60,000-70,000 units but

the total dosage administered was between 200,000 to 250,000 units

*General treatment* —A well ventilated dark room is quite necessary and noise is to be strictly excluded. It is only for this reason and no other that we treat our tetanus cases in special ward and not in the general medical wards. Proper feeding of the patient is quite necessary, owing to trismus and sleep from narcotic drugs, feeding is neglected in many cases. We always aimed at giving concentrated small feeds. In some cases nasal feeding was the method of choice. Proper position of the patient, particularly in elderly people is necessary and we must avoid patients injuring themselves against the sides of the bed or wall when convulsive. One other point worth mentioning is the avoidance of overdistention of bladder and loaded bowels. Proper rest, good sleep and avoidance of convulsive seizures are necessary. Our routine is to use a mixture containing bromide, chloral and cannabis indicum. It is palatable, soothing to many a patient and gives comfort to most. But we have to use other more potent remedies many times, both to induce sleep and treat and avoid convulsive seizures. The drugs commonly used in my ward are (1) Dial, (2) Somnifaine, (3) Paraldehyde and (4) Luminal. Evipan was never used as it was unobtainable. Dial or somnifaine or both combined were used to produce sleep, but the drug most extensively used was paraldehyde. It was used to prevent seizures and induce sleep. It was administered as an enema with olive oil. We used to give about four drachms of the drug in two ounces of the oil. But it should be given very slowly and the lower bowel must be empty before giving it. So it requires supervision. Besides olive oil becomes expensive when used extensively in the ward. So we began giving paraldehyde intramuscularly. The dose selected for an adult is about 8 c c. The site chosen is either the gluteus or the vastus externus muscle. If necessary it may be repeated within a few hours. The only drawback, whilst administering the drug in the muscle is the pain at the site of injection. This pain may last for some hours after the injection. Apart from this, it has never produced in our series of cases any untoward manifestation like respiratory paralysis or urinary changes after absorption. I am aware that some cases of neuritis when a nerve is involved are described, but we have never seen this complication in our series. It has one other advantage, that it needs no sterilisation.

In this series of 319 cases we never used any carbolic acid or magnesium sulphate to control convulsions.

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#### DISCUSSION

Dr B B Yodh said that the mortality rate was not improving in recent years. Large number of cases were necessary for proper statistics in evaluation of results. The pathology of tetanus was still an open question and recent work had sought to disprove the older

theory The tetanic spasm is a whole body twitch and not like an ordinary convulsion He was of opinion that large doses of serum should be tried in those cases that carry a heavy mortality as nothing much is known as to the site and amount of toxin formed Nursing must be improved in order to lower the mortality

**Dr R N Cooper** wanted to know if Dr Sahlar had any figures indicating the extent of the prevalence of post-operative tetanus Further he wanted to know if in Dr Sahlar's series there were many cases of tetanus developing from burns resulting from fire crackers American books have described 4th July tetanus as a distinct entity

Dr Cooper quoted the work of Abel from Johns Hopkins University who had observed that once the tetanus toxin fixed itself to the anterior horn cells, it produced a secondary toxin This secondary toxin killed the experimental animal by paralysing the respiratory centre No amount of antitoxin could neutralise this secondary toxin Hence Dr Cooper argued that the large percentage of deaths resulting from pulmonary complications in Dr Sahlar's series should not be looked upon as complication but as a termination resulting from secondary toxins

**Dr P K Sen** wanted to know the incidence of local tetanus

He quoted a case of facial palsy or facial tetanus He also desired information about the relation of the site of injury to the incubation period He gave an account of 17 cases of tetanus treated with sodium evipan, 2 cc intravenously 3-hourly There were 14 recoveries He suggested deep x-rays for local use on the line of treatment of other anaerobic infections like gas gangrene

**Dr S G Joshi** inquired about the number of cases that developed tetanus after having received a prophylactic dose, and if so how differently these cases behaved as compared to cases who had no prophylactic injection He related 2 cases seen by him of compound fractures who had received prophylactic doses and developed tetanus 10-15 days after admission These cases required very small doses of antitoxiserum to control the disease

**Dr. V N Patwardhan** said that the figures for mortality given in tables, especially those in Tables III and VI were likely to convey a wrong impression The death rate in each of the groups was bound to be influenced by factors such as (1) Incubation period (2) Duration of disease before treatment (3) Onset of complications, etc Unless all these factors were considered in arriving at mortality rate no correct impression could be conveyed by such tables Further Dr Patwardhan called attention to the fact that the paucity of notes regarding incubation period and period of onset in the case history, was not entirely due to the indifference of the houseman or the student but also due to the fact the patient himself or the relations accompanying him did not give any reliable information

Referring to the observation of Dr Yodh that he had treated 400 cases of tetanus in which the anti-toxin was administered intrathecally and that he wished to try another 400 cases by the intravenous administration of the anti-toxin in order to compare the relative merits of the 2 methods, Dr Patwardhan said that this

method of obtaining results was not altogether faultless. A better method would have been that of referring alternate cases for treatment by two methods which were to be compared.

Dr Patwardhan also suggested that any bland refined oil may be tried in place of olive oil to dilute paraldehyde for rectal administration.

Dr J C Patel put the following questions to the speaker: (1) How much of serum used in these cases was of European manufacture? This question was asked because before and during the early part of the war, serum sold by the Haffkine Institute was not manufactured by them. (2) Why an uniform dose of 250,000 IU was used in all cases regardless of age, sex, site of injury and severity of cases? Would the speaker increase the dosage in those cases where the symptoms of irritability persisted for 8 days or more? Dr Patel requested the speaker to study his cases from the point of view of the length of time the symptoms persisted after beginning the treatment.

Dr R G Dhayagude drew attention to the fact that in none of the samples of catgut sent to him from cases of post-operative tetanus were the tetanus bacilli. He concluded that the cause in these cases must be searched for somewhere else.

Dr. A. V Baliga was very keen on finding out and incriminating etiological factors in the group of post-operative tetanus, such as material used, presence of infection, whether the operation involved opening of the bowel or not. Hence he requested Dr Sahar to elicit details along these lines. He had seen cases of post-operative tetanus where no catgut was used and also where there was healing by primary intention. He had sent samples of contaminated catgut, twice to the Pathology Department and on both the occasions the report was negative.

Dr A V Baliga asked Dr Sahar about cases of tetanus following quinine injections. He also described one case of tetanus following quinine injection and another after solvochin injection, both the cases proving fatal.

Dr K. G Munsiff asked the speaker about the relative incidence in males and females. He related 5 cases of post-operative tetanus under him during the last 15 years. In one case it occurred after hernia operation, 21 days later. In one it occurred after the removal of the appendix. Three cases followed operations for piles. In the last 3 cases silk was used. In piles cases tetanus was noticed on the 5th day, treatment was immediately started, and the patient recovered.

Dr J. K Mehta asked: (1) Why do patients get facial paralysis following local injury over the face in a case of facial tetanus whereas we do not get paralysis of any other muscles in a case of ordinary tetanus? (2) We have given serum for the first 2 or 3 days and then do not give any serum at all. Is this sufficient to desensitize the patient or is it necessary to give a small dose of serum on the 6th or 7th day to desensitize the patient?

Dr A E DeSa said that there had been a great increase in the



incidence of post-operative tetanus in the post-war period. He could remember off hand at least four cases, all of which except one had proved fatal. He could not say where the blame for this complication lay but he had made it a practice to inject 3000 American Units of anti-toxic serum in a single dose as a pre-operative prophylaxis, where the use of catgut was contemplated and especially before ano-rectal operations.

**Dr P. Raghavan** said that Beckman and others who have treated cases of tetanus have divided them into three groups (1) A group that recovers even if nothing is done, (2) a group where everything is done but the patient dies, and (3) a group where the results depend upon the therapeutic enthusiasm.

**Dr Raghavan** said that it was advisable to treat mild cases with the doses advocated by **Dr Sahlar** and in severe cases as judged by the site of injury, extent of injury, days of duration and clinical picture, it may be worthwhile giving much larger doses of serum. He concluded that by such a procedure the mortality rate may be further reduced.

Yet another suggestion put forth was the local treatment of the wound with sulphanilamide group of drugs.

In summing up the discussion, **Dr. A. Hameed** drew attention to the following facts: 1 Uncertainty of incubation period. 2 Best way to judge the prognosis is to estimate the interval from 1st symptoms to the 1st spasm, period of onset. 3 Intravenous administration within first 24 hours, of 150,000 to 200,000 units of antitoxin. 4 No advantage gained by giving serum intrathecally. 5 Importance of Mag Sulphate as an anti-spasmodic. 6 Estimation of blood-anti-toxin in patients who recover and in those who die.

# Critical Notes and Abstracts

## INSULIN ALLERGY

In the recent study of allergy to insulin reported by Goldner and Ricketts, the term "allergic" is used as referring to symptoms which are due to the antigenic property of insulin as a protein substance. The words sensitivity and insensitivity are employed as referring to the varying degrees of body response to the specific metabolic function of insulin as a hormone. About 20 per cent of all persons treated with insulin, they say, have been reported as showing mild and transient reactions. In a few, however, the local reactions increase in severity, extend in size and spread over the body causing generalized urticaria with involvement of the mucous membranes, with severe pruritus, joint pain, headaches, elevated temperature, and circulatory and gastrointestinal symptoms. These reactions usually develop over a period of several hours and may persist for more than one day. They do not subside spontaneously with the continued use of insulin, but require desensitization or the cessation of insulin treatment.

Goldner and Ricketts report observations and immunologic studies on eight personally observed cases and 15 from the literature. The clinical histories, the positive skin tests with all different brands of commercial insulin, as well as with human insulin, and the results of passive transfer tests seem to prove that their patients belong to the group of persons with generalized allergy against the insulin protein itself. Furthermore, the observations indicate that this condition occurs predominantly in persons of the middle—or high—age group with moderately severe diabetes. Interrupted insulin treatment seems to predispose to allergy, they conclude. Intramuscular administration of insulin, treatment with calcium, histamine, histaminase and epinephrine have been recommended for therapy, as well as specific desensitization. The desensitization is performed either by giving multiple graduated doses of insulin at short intervals over a period of several hours, or by giving a small insulin dose a short time before the therapeutic dose is injected. They believe that skin tests may be advisable in all patients who resume insulin treatment and in those who have clinical symptoms suggestive of insulin allergy (Goldner M G, and Ricketts, H T *Journal Clinical Endocrinology*, 1942).

## GASTRO-INTESTINAL ALLERGY

Brown, A and Brown, F, *Med Clinics of N Am*, 26:37 1942

An individual is said to be allergic if he reacts to a substance in a manner different from the ordinary or normal person. Gastro-intestinal allergy is more frequent in infants and children, reflecting their greater susceptibility to food sensitivity.

All allergic patients have a threshold of sensitivity. It requires exposure to a certain amount of a substance to which a person is

sensitive before symptoms ensue This threshold tends to vary in different individuals This threshold may be altered by emotional states

The site of allergic reactions depends on the presence of antibodies in the tissues, such tissue being known as shock tissue A reaction is characterized by oedema producing swellings similar to urticarial wheals and secondarily by associated muscle spasm The latter results in changes in tonicity and motility of the small and large bowel More severe reactions show evidence of increased vascular permeability in the appearance of mucosal and sub-mucosal haemorrhages

Allergy in humans, often called atopy, has certain characteristics and these are 1 Sudden onset 2 Attacks of short duration 3 Abrupt cessation 4 Periodicity—the most important characteristic 5 A family history of allergy in over half the cases 6 Eosinophilia in the blood and tissues 7 A favourable response to injections of epinephrine 8 Positive skin reactions, in about half the cases

Allergic reactions in the oral region may be cheilitis, herpes labialis, canker sores and stomatitis Dysphagia, sensation of constriction in passage of food after swallowing the globus hystericus suggest reaction in the oesophagus

Distention, heartburn, epigastric distress, anorexia, epigastric pain, nausea and vomiting can be produced by allergy Ulcer-like symptoms are repeatedly found

The authors believe that when the site of the allergic reaction is in the small and large bowel, there is frequently abdominal pain, tenesmus, constipation, diarrhoea and bleeding This type frequently produces well defined syndromes, such as mucous colitis in the milder cases and chronic ulcerative colitis in the more severe ones Allergy may be the cause for the syndrome of appendicitis, of puritis and and pseudocholecystitis

In children gastro-intestinal manifestations of allergy may occur very early, they may even start when the child is on breast feeding The authors depend on the following for a diagnosis

- 1 A complete and careful history with special reference to the family and personal history of allergy
- 2 Skin tests
- 3 Trial diets, exclusion diets and food diaries

The authors show an example of their food diary which is a record of every food or medication ingested for at least a month By noting the relationship between the gastro-intestinal symptoms and the ingestion of certain substance, the aetiologic factor may be discovered

The treatment of gastro-intestinal allergy due to foods or drugs is the elimination of the offending agents Complete elimination of one or two foods is easy but when many food factors are found, difficulties arise In those patients who show many positive skin reactions the elimination of all possible factors may lead to malnutrition

It is important to test and re-test the food factors. For control of symptoms by medical means, antispasmodics and dilute hydrochloric acid are of some use. Only some patients can be well controlled by ephedrine sulphate.

## SULFA SENSITIVITY

Americans were sharply warned some time ago by Dr Robert P Fischells, Secretary and Chief Chemist of the New Jersey State Board of Pharmacy, against side-stepping their doctors to treat their own ills with sulfa drugs. And a just-published text<sup>1</sup> by Dr Bret Ratner, professor of pediatrics at the New York College of Medicine, shows that the warning has more behind it than the mere fear that careless self-medication might make people sick.

Experience with the sulfas has taught doctors that patients can become allergic to the drugs—which means that a person who has had them once may not be able to take them again. For example, the man who uses sulfanilamide for a cold-cure risks his chance of pulling through pneumonia or meningitis later, hence, if too many people began to stock their medicine cabinets with the sulfas, misuse of the drugs in minor illnesses would become a grave threat to medicine's best weapon against deadly diseases.

Though the field of sulfa allergy is so new it is not fully charted. The Journal of the American Medical Association has reported that 'approximately one-third of all patients treated with sulfonamide drugs develop a sensitivity sufficient to interfere with their subsequent use on these patients.' Symptoms of sulfa-sensitivity vary in different patients, but danger signals for which doctors watch, are a rash, fever (which may reach 106), chills, weakness, and prostration.

In 1941 United States production of the drugs totalled approximately 750,000 pounds of sulfapyridine, 1,200,000 of sulfanilamide, and between 1,000,000 and 1,500,000 pounds of sulfathiazole. Since relatively little of this tremendous output was shipped abroad, doctors estimate that between ten and fifteen million Americans were treated with the sulfas in 1942. Countless lives were saved, but—according to the Americans Medical Association estimate—from three to five million of people treated also became sensitized to the sulfas.

To date doctors have discovered no sure way to forestall sulfa allergies, but, according to the Ratner book, wise planning can at least keep the reactions at a minimum. On this score Dr Ratner's first dictum is that since the sulfas are the doctors' trump, using them for minor ailments is like wasting aces on tricks that a deuce would take.

For those who become sulfa-sensitive in spite of precautions, Dr Ratner notes the encouraging fact that a person may be allergic to some of the sulfa compounds without necessarily being sensitive to the others. Before doctors can take full advantages of such differential allergy, tests will have to be devised to show which people are sensitive to which drugs.

## THIAMINE ALLERGY

Leitner describes (*Lancet*, Oct 16, 1943, 2 474) untoward effects of vitamin B<sub>1</sub> in two patients. A man of 71 who had taken injections of vit B<sub>1</sub> some years previously without any mishap was taking injections of 20 mg of thiamine chloride repeatedly during the last 3 or 4 weeks. He developed restlessness, exhaustion, insomnia, itching and depression. Later he developed asthmatic attacks with sneezing, palpitations, and extreme anxiety. The physical examination showed nothing except eosinophilia of 34.5%. His first asthmatic attack began 7 hours after a fourth injection, and a very serious attack one hour after the fifth injection. Skin tests with vit B<sub>1</sub> produced a wheal of about 2 cm in diameter. On stopping the drug and auto-haemotherapy the attacks disappeared, the eosinophils fell to normal and skin tests were negative after 4 weeks. A woman of 42 was having large doses of vit B<sub>1</sub> injections. She showed excitement, tremor, insomnia, in spite of large doses of sedatives day and night, headache, palpitations and giddiness. All these symptoms disappeared on discontinuing the drug.

The untoward effects are either allergic or similar to a thyrotoxic state. Many cases of allergic manifestations after thiamine are recorded in literature, including a case of sudden death. The sensitiveness develops gradually. The incubation period always exceeds 7 days. When injections were given at intervals of less than 7 days anaphylactic reactions were small or absent and most severe reactions followed intervals of 10 and 9 days. The symptoms resembling thyrotoxicosis—excitement, tremor, fatigue, insomnia, giddiness,—seem to suggest simple overdosage.

## INTOLERANCE TO LIVER EXTRACT INJECTIONS

Elizabeth Delikat reports (*Brit med J* 1 539, May 1, 1943) three cases of pernicious anaemia in which the patients had become sensitive to parenteral injections of liver extract. Generalised urticaria, itching, puffiness of face, loss of speech, failure of vision, and sudden collapse were some of the manifestations. Intradermal tests with liver extract may give positive reaction but not always and she emphasises that the skin tests cannot be relied on to indicate tolerance in these cases. Stoppage of the liver injections and desensitization with fractional doses are advised to avoid a sudden anaphylactic shock and death. Desensitization is carried out with 0.05-0.1 cc liver extract solution, injected every other day with increments of 0.1 cc at each successive dose, until a dose of 1 cc is reached. The patient should be under observation for two hours after each injection until he tolerates 3 cc in one dose. Then the dose may be increased by 0.5 cc at two week intervals until 4 cc could be given in a single injection. This may be continued as a maintenance dose every four weeks. Minor symptoms such as headache, itching, or swelling of the forehead may be alleviated by oral ephedrine. Calcium and adrenalin are necessary for severe reactions.

## EARLIER DIAGNOSIS OF TUBERCULOSIS BY GUINEA-PIG INOCULATION

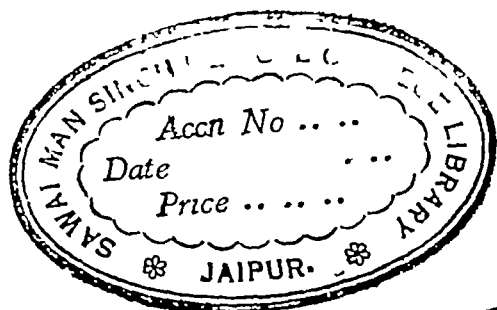
Woolsey Carrie I : A More Rapid Method of Guinea Pig Inoculation for the Diagnosis of Tuberculosis, *J Lab & Clin Med*, 24 855 (May) 1930

Shortening of the time necessary for the diagnosis of tuberculosis will make this diagnostic aid of greater value. Woolsey, Department of Pathology and Bacteriology, Cook County Hospital, Chicago, has described an intracutaneous method that has shortened the time for diagnosis to three weeks in comparison with the six to eight weeks by the older subcutaneous method.

A small area on the side of the abdomen of a guinea-pig is first shaved, then 0.4 cc of the infective material is injected intracutaneously. Within seven to twenty-one days, or in unusual cases, longer, a nodule appears at the site of the injection, which averages about 2 mm in diameter. The nodule should be incised and smears examined for the presence of acid-fast bacilli. Each guinea-pig should be observed weekly and notation made indicating its condition. A closed nodule may become crater-like should two weeks pass between examinations, and consequently it can more easily and definitely be proved positive. However, the earlier diagnosis would be missed by delay. It should be noted that the early smear may demand a reasonable period of search to find the organisms. Occasionally, the third or fourth examination of the pustule must be made before organisms are found. As soon as the inguinal lymph nodes have enlarged on the side of the injections, the guinea-pig may be killed, and an autopsy performed to verify the early report.

Secondary invaders in the exudates have not killed any pigs nor interfered with the development of tuberculous lesions at the site of intracutaneous injection except in the case of sputa. A small abscess soon develops in such cases, from which staphylococcus aureus, hemolytic streptococci, and bacillus coli among others have been isolated. Occasionally, acid-fast bacilli have been found even in this early abscess, but the author states that more often the abscess heals over readily and is followed by the later nodule from which only acid-fast bacilli are recovered.

In the total number of 173 guinea-pigs included in Miss Woolsey's series, tubercle bacilli were recovered 72 times, or in 40 per cent of the exudates studied. Twenty-seven different human exudates were investigated.



# A review

## PENICILLIN ITS PROPERTIES AND POWERS AS A THERAPEUTIC AGENT

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The chemotherapy of bacterial infections, which had been little more than an ideal until 1935, became a reality with the advent of prontosil. During the rapid development of sulphonamide treatment which followed, other organisms than *Streptococcus pyogenes* were found to be susceptible, and successful attacks on *Gonococcus*, *Meningococcus* and *Pneumococcus* followed in swift succession. It seemed likely at one time that with the advent of new drugs of this type all bacterial infections could be brought under control. This hope has been disappointed, and for some years we have been discovering the limitations of sulphonamide treatment rather than extending its scope. Even among the most susceptible bacteria some strains occur with exceptional resistance to the sulphonamide drugs, while there are many species relatively or wholly resistant to them.

Another great therapeutic discovery has now been made, which provides a remedy for some of the infections in which sulphonamides fail. That it will do in certain cases what these drugs will not is only part of its claim to our interest. It is a substance with hitherto unheard of—almost unimagined—properties. It combines enormous antiseptic power with such a degree of freedom from toxicity to the mammalian body that one thousand times the concentration necessary for therapeutic action can be produced in the blood without ill effect. Such a combination of deadliness to bacteria with harmlessness to the body is more than the most sanguine chemotherapist can have pictured as possible before the properties of penicillin became known. Treatment with it is governed not by the fear of over-dosage, but only by anxiety to employ so precious a remedy with the utmost possible economy.

It is my task to present a general picture of what penicillin now is and what it will do. Penicillin is now being produced on a considerable and rapidly increasing scale, in both England and the U.S.A., by extraction from mass cultures of *Penicillium notatum*. No other method of production is yet known, although synthesis is an eventual possibility. In each of these countries the output has been officially controlled, and supplies have been afforded for clinical trials only to chosen investigators. In England not only the original employment of penicillin as a therapeutic agent but much of the subsequent study on which our present knowledge is based has been due to the enterprise of Florey himself and his colleagues.

### THE PROPERTIES OF PENICILLIN

Penicillin is an unstable acid, and the preparations used in therapeutics are its salts. The sodium salt employed for systemic treat-

ment is hygroscopic and somewhat less stable than the more easily handled calcium salt, which is used mainly for local application. Potency is expressed in Florey [Oxford] units, an arbitrary amount determined by comparison with a standard preparation. Pure penicillin would have a potency of at least 1,000 units per mg, that in present use is far from pure—owing to the serious loss of active substance which further purification entails—and material with a potency of 100 units or less per mg is quite satisfactory for clinical use. It has been shown experimentally that an increase in purity diminishes toxicity, and clinical experience has shown that untoward effects such as pain in intramuscular injection and fever or thrombophlebitis following intravenous administration are caused mainly by products of low potency. These effects are thus due to impurities rather than to penicillin itself.

In the presence of penicillin, even in very low concentration, certain species of bacteria not only cannot multiply but slowly die. Whether this effect is "bactericidal" or purely "bacteriostatic" is not clear, the distinction is not easily made, and the mechanism of the effect is unknown, although the peculiar changes in bacterial morphology first observed by Gardner suggest that at least the process of division is inhibited. More important from the practical standpoint is the fact that this effect is exerted as well in serum, blood, or even pus, as in a simple medium such as broth. Within wide limits it is also independent of the number of bacteria present. Yet even very high concentrations are without effect on the activity of leucocytes both by this form of study and by several others. Penicillin has been shown to have almost no local tissue toxicity. These facts explain the superiority of penicillin over sulphonamides for direct application to wounds, concentrated sulphonamides are by no means altogether non-toxic, they are far from indifferent to bacterial numbers, acting best when only few are present, and they are inhibited by the breakdown products in pus. Penicillin overcomes all these difficulties, and the consequent difference in effect is fully equal to expectation.

It is essential to understand that penicillin exerts this action only on certain species of bacteria, it is indeed the most highly selective antiseptic known, and for years was used by Fleming as an agent in selective culture media, which prevented the growth of some bacteria and permitted that of others. Most of the susceptible species are gram-positive, they include the three main pyogenic cocci (*Staphylococcus*, *Pneumococcus* and *Streptococcus pyogenes*), the gas gangrene group (among which *C. oedematiens*, although resistant to sulphonamides, is almost as susceptible as *C. welchii* to penicillin), *B. anthracis* and *C. diphtheriae*. The only fully susceptible gram-negative species are *Nesseriae*, the gonococcus and meningococcus. Among resistant organisms are the tubercle bacillus and almost all gram-negative bacilli, including the typhoid-dysentery group (some of which are slightly sensitive), the genera *Brucella* and *Haemophilus*, and two frequent wound invaders, *Proteus* and *Ps. pyocyanea*.



## SYSTEMIC PENICILLIN TREATMENT

Penicillin can be used therapeutically in two ways. It can be applied locally, or administered by parenteral injection so that it circulates in the blood and reaches every part of the body. The former method is economical but often difficult and sometimes inapplicable, the latter sure in its effect but immensely costly, using as a rule at least fifty times the amount needed for local treatment. Penicillin is absorbed from the alimentary tract, but cannot be given by this route because much of it is destroyed by acid in the stomach or by bacteria during rectal infusion. It must therefore be injected, either intramuscularly or intravenously. Unfortunately it is rapidly excreted in the urine, and the maintenance of an adequate blood level has been aptly compared by Florey to an effort to keep a bath full with the plug out. Such a level can, however, be maintained by continuous intravenous infusion or by intramuscular injections at intervals of not more than three hours day and night, the daily dose for an adult being about 120,000 units. This may have to be continued for seven days or even longer. A sudden and dramatic improvement is rarely seen, and sustained treatment, arduous for those in charge and disagreeable for the patient, is the price of success.

In present circumstances it is unjustifiable to administer penicillin systemically for any condition amenable to sulphonamide treatment. Septicaemia due to *Strept. pyogenes* or *Pneumococcus* is therefore treated only in the exceptional cases found to be sulphonamide-resistant. Staphylococcal septicaemia is always relatively resistant to sulphonamides, and penicillin, when available, is more decidedly indicated for this condition than for any other. Apart from septicaemia, extensive and deep-seated infections inaccessible by local applications require systemic treatment, these include osteomyelitis, severe cellulitis and gas gangrene. It has recently been shown by Florey and Cairns in battle casualties from Sicily that potentially infected compound fractures can be closed with the aid of this treatment. American experience suggests that sulphonamide-resistant pneumococcal pneumonia will respond to a very short course, and observations made in both the American and British armies have shown that cases of gonorrhoea can be cured by a total dose of little more than 100,000 units given in a space of about 24 hours. With more experience and larger supplies, further and more precise indications for this form of administration will doubtless be obtained.

## LOCAL PENICILLIN TREATMENT

The local application of penicillin takes many forms, some calling for ingenuity which is well rewarded by the remarkable effects to be obtained at little cost. Application to burns and other superficial and accessible wounds is secured by a cream or powder, the only satisfactory diluent known for the latter being sulphanilamide. These preparations can be relied on to eliminate infection by haemolytic streptococci and staphylococci from such areas. Similar applications are highly successful in the treatment of skin infections such as impetigo and sycosis barbae. The treatment of deeper wounds

demands arrangements whereby a preparation can be enabled to penetrate them completely and persist there. A radical change in surgical technique is often necessary to secure this. Thus an abscess cavity or other infected area which would normally be laid widely open and drained freely may either not be incised at all but treated by aspirations and injection of penicillin solution, or if incised, it may be sutured again and closed, except for a small aperture containing a tube through which the solution is introduced at intervals afterwards.

The various applications of this principle are too numerous to detail here. Historically the first was the modified operation which enabled the Floreys to treat mastoiditis, and the latest, and at present the most important, is the closure of recent soft-tissue battle wounds advocated by Florey and Cairns on the strength of their recent experience in North Africa. Much more remains to be done in devising methods of using penicillin to good effect locally in the infinite variety of wounds, sinuses and other lesions to which it can be applied.

Common causes of failure are morbid anatomical conditions such that the solution either does not reach all parts of the lesion or does not persist there, the presence of bacteria which are resistant to penicillin or actually destroy it, and antecedent fibrosis mechanically preventing closure and healing.

A special example of local treatment is the intrathecal injection of penicillin solution for the treatment of meningitis. This has been highly successful in a few cases, and is imperative for treating this condition, since penicillin, unlike the sulphonamides, does not pass freely from the blood into the cerebrospinal fluid.

#### FUTURE PROSPECTS

The time may not be very far distant when penicillin will become generally available, at least in limited quantities. This will certainly happen soon after the war is over, when military surgery, which now has priority over other demands, no longer calls for a large supply. It is therefore perhaps not too early to issue a warning that the successful use of penicillin is by no means as easy as treatment with sulphonamides. It has so far been exclusively in the hands of experts under research conditions, who have obtained good results only by unremitting care and with the aid of strict laboratory control. The duties of the laboratory in connection with penicillin treatment are very onerous. It is necessary first to determine the nature of the infection and the sensitivity to penicillin of the organisms concerned. Local treatment should then be controlled by frequent further cultures. Systemic treatment calls for repeated estimations of the penicillin content of the blood in order to verify adequate dosage. Owing to its instability and liability to contamination with resistant bacteria, penicillin should also be dispensed by the bacteriologist rather than the pharmacist. Without such services in addition to expert surgical and nursing care, any but the simplest forms of penicillin treatment may easily fail.

Looking further into the future, it may be asked what prospects there are of extending the scope of this treatment. The full possibilities of penicillin itself have not yet been explored, even in infection by bacteria known to be susceptible. For example, little is yet known about its effect in gas gangrene, and still less about syphilis, diphtheria or anthrax. But is there any possibility that substances related to penicillin has little or no action? A systematic study of other moulds has been in progress for several years, and so far none has been found which produces an antibacterial substance equal in therapeutic value to penicillin, although hundreds of species have been tested. Some of these substances do, however, act on a wider range of bacteria including gram-negative bacilli. This property has not yet been found uncombined with toxicity to mammalian tissues. The other possible approach is the synthetic. When the structure of penicillin becomes known it may be possible so to vary it that a wider range of activity is secured. One thing quite certain is that penicillin differs fundamentally from other antibacterial agents. Its discovery is an achievement of the first magnitude, of which the ultimate consequences cannot yet be foreseen [B.M.B. 1971]

## CLINICAL USES OF PENICILLIN

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The successful application of experimental laboratory work to therapeutic measures could hardly be better exemplified than in the case of penicillin. Before any trial was made on man, almost the full range of infections capable of response to the drug was known. Equally important was the knowledge that the upper limit of dosage was not likely to be influenced by any toxic effect. Among the other inferences of practical importance that could be made from the laboratory work were that oral administration of the unprotected drug would be ineffective because of its inactivation by the acid gastric juice, that frequent administration would be necessary because of the rapid concentration and excretion of penicillin by the kidneys, that it would be unwise to prepare wounds for local application by cleaning with a number of the common antiseptics because of the inactivation of penicillin by heavy metals and by oxidation. The lack of any inhibitory effect on leucocytic activity by therapeutic concentrations of penicillin indicated that the disappearance of pus from lesions infected only by sensitive organisms would probably be a fair criterion of the elimination of sepsis.

With these facts already known, the main points still to be elucidated when clinical trials were begun were adequate dosage, frequency and routes of administration and the most suitable methods for local application.

## CLINICAL TRIALS

The earliest clinical trials, which included some 200 cases, were instigated by the *Sir William Dunn* School of Pathology, Oxford (Abraham, Chain, Fletcher, Florey, Gardner, Heatley & Jennings,

1941, Florey & Florey, 1943) They demonstrated the therapeutic effectiveness of the drug by both systemic and local administration. The cases chosen for treatment were pyogenic infections falling into the following categories

Generalised infections accompanied by local lesions in bones, lungs and heart valves	Chronic blepharitis
Acute mastoiditis	Chronic sinus infections
Infections of the skin	Empyema
Infections of the conjunctiva, cornea and lacrymal sac	Synovitis
	A miscellaneous collection of infective conditions

The causal organism in the majority was the staphylococcus, in others it was the streptococcus or a combined infection by both organisms. A few infections were pneumococcal, gonococcal or due to actinomyces, and occasionally no organism sensitive to penicillin could be isolated.

The results of these early trials at Oxford may be summed up as

Complete recovery	143 patients
Improvement	43 "
Little or no response	14 "
<i>Total</i>	<hr/> 200 <hr/>

These results appear striking enough to merit some consideration of the criteria adopted in ascribing recovery specifically to penicillin treatment. The first criterion was bacteriological. Pyogenic organisms present in lesions became scanty during treatment and eventually disappeared. If, concurrently with their disappearance, the local and general signs of inflammation subsided, function returned and healing began, these effects were considered as fairly attributable to removal of infection by penicillin. The fact that most patients treated in the first year or two of clinical trials were considered moribund, had not responded to any other treatment, or suffered, from an infection which has persisted for many months or years without improvement, gave additional support to the conclusion that penicillin was the instrument whereby recovery took place.

About 150 cases of burns were also treated at about this time by Dr Colebrook working for the *Medical Research Council* in the Burns Unit at Glasgow (Clark, Colebrook, Gibson, Thomson & Foster, 1943), and Flight Lieutenant Bodenham (Bodenham, 1943). No staphylococcal or streptococcal infection of a burn failed to disappear under adequate treatment. Healing was accelerated or successful skin grafts were carried out following the removal of the organisms from the surface of the burn.

Work in the U.S.A. has confirmed and amplified the British results mainly in systemic treatment (Keefer, Blake, Marshall, Lockwood & Wood, 1943). Of 500 cases reported, including some where the infection was not the only pathological condition (some cases were also

suffering from cancer, aplastic anaemia, aneurysm, etc.) the results were

Recovery or improvement	366
No response	40
Deaths	94
<i>Total</i>	<hr/> 500 <hr/>

This series included 129 cases of gonorrhoea, of which the treatment was uniformly successful and subsequent reports (*Lancet*, 1943, Garrod, 1943) have confirmed the very rapid response to treatment in this condition irrespective of whether the infection is sulphonamide-resistant or not. Pneumonias were also treated with success, but the results recorded were by no means so striking as in gonococcal infections.

In neither the British nor the American series did recovery occur in subacute bacterial endocarditis (*Streptococcus viridans* infection) even after prolonged treatment.

In England, following the earliest trials, it was thought advisable to carry out a comparative trial of acute infections from which patients would in any event recover. By comparing penicillin-treated cases with similar acute infections treated by current methods the effects which might be attributable to the drug could be gauged.

Infections of the hands were chosen for this trial (Florey, M E & Williams, 1944). A hundred "control" patients were treated by recognised methods and a second 100 were treated in every way similarly except that penicillin was applied locally from operation onwards in place of (usually) hypochlorite preparations and (when considered necessary) sulphonamides by mouth. Bi-weekly bacteriological examinations showed that, in 75% of control wounds, pyogenic organisms persisted from the first incision until complete healing. The remaining 25% lost their infection or showed a diminished growth only when healing was far advanced. In 95% of the penicillin-treated cases, these organisms had markedly diminished in numbers or had disappeared before the end of the first week.

From the clinical point of view this rapid elimination of sepsis resulted in the following marked differences.

<i>Control</i>	<i>Penicillin Treated</i>
Continuance of pain and throbbing for variable periods following incision	Almost invariable relief of pain from incision and first application of penicillin onwards
Production of pus until healing was well advanced	Pus scanty or absent following operation
Formation of much granulation tissue with consequent contraction, limitation of movement, and sometimes painful scars	Little formation of granulation tissue Rapid and more complete restoration of movement and smooth and painless scars
In severe infections, usually much sloughing, death of tendons and bone, and loss of digits	No loss of digits or any other tissue when treatment was begun at first operation

The retention of digits and restoration of function are particularly valuable assets in an industrial community where early return to work depends on full use of the hands. The working time saved to the 100 penicillin-treated cases totalled in the aggregate a number of years

A further series of cases has been treated in the war zone (*Lancet*, 1943, Garrod, 1943). Here local application of the drug has enabled the early suturing of war wounds of the soft tissues to be carried out with almost uniform success. In no case did deleterious results follow this unorthodox treatment, although in some wounds complete union was not achieved and a few broke down. Results at 3 weeks were

Complete union	104
Subtotal union	60
Failure	7
<i>Total</i>	<hr/> 171 <hr/>

In wounds complicated by compound fractures systemic as well as local treatment was employed, but the results were not so strikingly successful as in the soft tissue injuries. Results are improving, however, with developments in technique and the earlier administration of penicillin.

Gas gangrene was treated in 7 patients. The systemic route was used. Four of these patients recovered, but further improvements in results may well follow adaptations in the method of administration.

Of the penetrating brain wounds treated, some had an established infection, while others were treated within a few days, at a stage when infection had hardly developed. Results were satisfactory and healing occurred without fungus formation in all but one case. Three out of the 23 patients died, however, but in two of these the infection by gram-positive organisms had been controlled and the third was inadequately treated.

This series of war injuries demonstrated well the successful and rapid results obtained when penicillin treatment is begun in the early stages of infection, rather than when the condition is so well established as to be less accessible either to local or systemic exhibition of the drug.

Investigations up to date have therefore shown the value of penicillin

i As a preventive of infection in wounds, enabling a potentially septic wound to be treated in much the same way as an aseptic one,

ii in the promotion of healing in burns and for ensuring the success of skin grafts,

iii in infections (due to sensitive organisms) either (a) chronic or (b) of such severity as to render the prospect of death likely which have not responded to other forms of treatment,

iv in acute infections due to sensitive organisms,

v in the rapid curing of gonorrhoea including sulphonamide-resistant cases,

vi in pneumonia,

vii probably in gas gangrene, but here numbers have been few and methods not fully tried out

#### SPECIAL CONSIDERATIONS

(a) *Excretion* Very early in the Oxford clinical trials the rapid excretion of penicillin by the kidneys was seen to be both a problem and an asset. In the days when every unit was precious, efforts were made to recover the drug from the patient's urine, but the labour and inconvenience were great and were justified only by the scarcity of material. The rapid deterioration of the penicillin when acted on by bacteria in the urine also made the yield very variable. One patient was able to pass urine every hour for 11 hours after a single dose. These specimens were assayed immediately and, although he was still excreting penicillin when the last specimen was taken, more than 75% of the dose was regained. Such was not the case when urine was collected in larger amounts and at longer intervals. Rammelkamp & Keefer (1943b), who have carried out detailed work on absorption, excretion and toxicity of penicillin, have also obtained variable yields from the urine, but it is not yet clearly established whether the total amount is excreted or whether part is destroyed in the body.

Its rapid elimination has been of value in determining the time taken for penicillin injected by various routes to reach the circulation and for a single dose to disappear. After intramuscular or intravenous injection, penicillin may be detected in the urine almost immediately, and after intrapleural injection within an hour. Penicillin is also concentrated by the kidneys, as after a single small dose it can be detected in the urine for well over 24 hours, even when the concentration has at no time been great enough to be detected in the blood by present methods. Administration for urinary infection has therefore been successful when repeated only once or twice in 24 hours, and staphylococcal and streptococcal urinary infections have been cleared up by doses which were relatively very small.

(b) *Effect on blood cells* On all cases treated from Oxford systemically and on many treated locally regular blood examinations were carried out. In no case was there a fall in the erythrocyte count during penicillin treatment, and in all severely ill cases, except one puerperal patient in whom a profuse lochia continued throughout treatment, there was an average rise of 250,000 to 500,000 erythrocytes per week. In view of the poor condition of myocardium in septic patients, there seems therefore to be little indication for adding the strain of blood transfusion to the work of the heart. The leucocyte count appeared to give a good indication of the progress of the treatment. If it was low from toxæmia (or possibly from previous sulphonamide administration) at the beginning, it began to rise within 24 hours. If high in response to infection it dropped steadily as the infection was controlled, but never below normal limits. The leu-

cocyte count should therefore come in prominence as an indication of progress, in treatment by penicillin, where the temperature chart often does not reflect improvement in the early stages

(c) *Accessibility of thecal and serous cavities* Passage of penicillin between the blood stream and serous cavities seems to be slight (Rammelkamp & Keefer, 1943a, 1943b, Fleming 1943, Florey, M E & Florey, H W 1943), and for treatment of infections of the meninges pleural cavity, joints and peritoneum local rather than intramuscular or intravenous injection is therefore indicated. The physiological basis of the apparent (relative) impermeability of these membranes to penicillin still remains to be elucidated

(d) *Toxicity.* Any signs of toxicity have been carefully sought by observation of the patient, by regular examinations of blood urea and urine, and by hæmatological examinations. Occasionally the blood urea has risen but it has fallen again on the day on which penicillin has been discontinued. No case in which albuminuria has developed has been recorded in the English series, but when present initially it has cleared up under penicillin therapy. Fever often increases when penicillin is first administered, but gradually subsides again. This rise of temperature may be due to a more rapid absorption of bacterial degradation products rather than to any toxic effect of the drug

(e) *Radiological findings* Special mention should be made of the radiological appearances of infected bone treated with penicillin. A very rapid rarefaction of the affected bone occurs, and radiography in less than a week, often in 2 to 3 days, suggests deterioration, whereas the clinical signs indicate that the septic process is under control. Further radiographs demonstrate the rapid reformation of bony tissue as compared with control cases, in which (in the series of hand infections) sequestrum formation occurred more often than not. In acute infections no sequestrum formation has been found in the English penicillin-treated series. If, in a chronic infection, dead bone has already separated before the beginning of penicillin treatment, rarefaction will occur around the sequestrum and will make its presence and site more obvious to the surgeon

(f) *Bacteriological desiderata,* Mention of the organisms sensitive to penicillin has been made elsewhere (Fleming, 1929 Abraham *et al*, 1941). It is clearly futile to attempt penicillin treatment when the organism concerned is insensitive. Emphasis has already been laid on the speed and completeness with which organisms usually disappear during treatment with penicillin. A few further points, however, should be borne in mind. Bacteria do not readily disappear from lesions if there is any dead tissue present such as a slough or sequestrum, nor do they disappear when access by the drug is not complete. This may occur with systemic treatment in undrained abscess cavities or in serous cavities, where the penicillin may be brought by the blood stream only as far as the periphery of the infected area. It may also occur with local treatment in sinuses which have not been completely opened up, or in septic areas where the incision has not reached the whole site of infection. Disappearance and elimination



of infection, therefore, depend on (a) a sensitive organism, (b) adequate dosage, (c) absence of dead tissue, (d) full access to the site of infection. It has not been uncommon to find coliform organisms appearing or increasing in number during penicillin administration, but they do not appear to affect the clinical course or delay healing materially, even when green or pinkish "gram-negative pus" is present

*In vitro*, bacteria readily become penicillin-resistant, and some clinical cases have been reported where resistance of the order of 4 to 8 times developed during treatment although clinical improvement continued (Florey & Florey, 1943, Rammelkamp & Maxon, 1942) Sulphonamide-resistant strains have been found, however, to be fully sensitive to penicillin

#### METHODS OF TREATMENT

(a) *Systemic administration.* In the early clinical trials the greatest difficulty encountered was to find the adequate dosage. The ring test (Abraham *et al*, 1941) was not sufficiently sensitive to demonstrate any bacteriostatic effect in the blood after doses which were believed on theoretical grounds to be large enough to produce bacteriostasis throughout the body. Eventually, after trial and error, a baby provided the foundation on which an adequate dose to eliminate infection was established as 1,000 units per pound [454 g] of body weight in 24 hours. Later, the more delicate slide-cell technique was adopted, in which the inhibition of bacterial growth by the blood serum could be accurately followed. This served to establish that intravenous or intramuscular injection should be repeated not less than 3-hourly, the standard single dose for an adult being 15,000 Oxford units. Later work by Rammelkamp and Keefer (1943b) has shown that even when nearly 3 times the dose is given there is no prolongation of the time during which the drug can be detected in the blood stream. Good effects have been produced in acute infective conditions by much smaller doses than 15,000 units in the Mayo Clinic (Herrell, Hellman & Williams, 1942, Herrell, 1943) and elsewhere, but although these results are very satisfactory it would seem wise for general use to recommend a dosage which has been found adequate in many conditions—acute, well-established, or long-standing—especially in view of the fact that organisms may become penicillin-resistant.

The *gastro-intestinal* route was tried—by mouth in specially prepared capsules to resist solution by the acid gastric juice, and by duodenal tube. Although some absorption certainly took place, the variable rate at which the drug was absorbed rendered the bacteriostatic concentration in the blood inconstant and uncertain when doses of a size which is at present practicable were used.

In the early clinical work, *subcutaneous* injection was avoided owing to the pain associated with it. Although according to the work of Rammelkamp & Keefer (1943b) there may be some advantage in using this route, as an adequate blood level is apparently maintained far longer than after intramuscular or intravenous injection, the large

volume they used was inconvenient and may explain the slow absorption

For the best results by *intravenous* use it is essential to use a pyrogen-free preparation (the pyrogenic impurity can be removed during purification) The penicillin may be given intermittently, or continuously by a "drip" infusion Thrombosis at the site of injection is common after a variable period of intravenous therapy, although with good samples of the drug the "drip" can often be continued for some days

For this and other reasons the *intramuscular* route was adopted for general use in the British work Providing a good technique is used, most samples cause little general or local reaction, but some samples have been encountered which do cause prolonged pain after intramuscular injection There can be little doubt that this reaction, the thrombosis after intravenous injection, and other reactions of a minor character are due to impurities As the penicillin used therapeutically is still far from pure, usually containing only 10-20% of the pure substance, it is to be hoped that the quality of penicillin produced for clinical purposes will improve By the use of the intramuscular route, material which causes a sharp rise of temperature on intravenous administration can be employed without causing a pyrexial reaction

(b) *Local administration* has been used extensively in Britain, largely because of the scarcity of supplies, but many instances might be given where it has advantages over systemic treatment Where an infection is definitely localised, and there is a surface or cavity which will retain a preparation of penicillin, a much greater concentration can be applied to the site of infection and, by using a suitable vehicle, the action of a single dose may be prolonged for as long as 24 hours For this purpose the following preparations have been found useful

i A dry calcium-penicillin powder of low potency (i.e. a relatively unpurified preparation containing a low percentage of pure penicillin)

ii A powder composed of a calcium-penicillin preparation diluted with sulphanilamide or sulphathiazole powder to a strength of 2,000 to 5,000 units of penicillin per gram Such a powder is very suitable for insufflation

iii Solutions in distilled water of 250 to 1,000 units per  $\text{cm}^3$

iv A paste made up of lanette wax SX, oil (e.g. castor or arachis) and water to which penicillin is added to a strength of 150 to 250 units per  $\text{cm}^3$  With this preparation the activity of the drug may be retained for at least 24 hours

v Mixed with vaseline or some other base as an eye ointment—500-800 units per  $\text{cm}^3$

Various methods of local application have been used, such as simple dressings impregnated with the paste preparation, insufflation of powder, or spreading of the powders over infected surfaces A method which, when applicable, is very effective because it embodies the principle of maintaining a close cavity, is to aspirate pus and inject

a solution by syringe and needle. An alternative method is to remove the purulent and damaged tissue from an abscess cavity or wound, suture the raw edges and insert one or more narrow rubber tubes (retaining them by a suture) leading down to the depths of the cavity. In the latter method, the cavity is aspirated and the penicillin solution is injected through the tubes by means of a syringe. One extremity of the tube projects through the dressings. Injections are made 6- to 12-hourly according to the acuteness of the condition, for a minimum period of 5 days.

Sinuses of many years' duration have been treated successfully by injection of the solution under pressure, thereby opening up their many ramifications. The mouth of the sinus is closed with a sterilised rubber bung in order to retain the fluid from one injection until the next. This retention of the drug continuously *in situ* over a period of time has been a cardinal feature of treatment. Because of its bacteriostatic rather than bactericidal action, time must be allowed for the inhibited bacteria to perish by phagocytosis or otherwise. Any temporary cessation of the inhibitory influence of penicillin may permit further bacterial proliferation and so prolong the time necessary to eliminate infection.

The duration of treatment has depended on the time taken to eliminate bacteria from lesions. There is no indication that increased dosage beyond the point necessary to secure complete bacteriostasis is of any value. The effect of higher dosage is merely to cause more rapid excretion of the drug by the kidneys. Bearing in mind the possibility that the pathogenic organisms may develop resistance to penicillin, a fully bacteriostatic dose should be given from the beginning. There has been little evidence, except in subacute bacterial endocarditis, that an infection by a sensitive organism will not respond to prolonged treatment. The point to be remembered is that treatment must be continued until all foci of infection have been removed. As mentioned earlier, when dead tissue is present, surgical removal may be necessary, but radiological and bacteriological findings are better indications for this than is the temperature chart.

#### ASSESSMENT OF PROGRESS

(a) *General infections* When treating a case with penicillin, assessment of progress is liable to be based on the signs familiar in sulphonamide therapy. This may, unfortunately, lead to erroneous conclusions. The temperature, for instance, in a case of osteomyelitis may assume a swinging character when penicillin is first given, and it never falls rapidly, as often occurs with the sulphonamides. Often the temperature mounts to a higher level than before treatment was instituted.

By the time the temperature has become normal, which may take from 2 to 3 weeks, resolution has largely taken place. The radiograph, which in infections of bone shows rapid and often startling rarefaction, should be regarded as evidence of the fast absorption of damaged bony tissue, and not of deterioration in the condition.

The earliest signs of progress are noticed by the nursing staff

Within a day or two the patient sleeps better, eats better and is relieved of much pain. Bacteriological examination carried out twice a week will reveal steady diminution and eventually total disappearance of the infecting organism, provided that the drug has full access, locally or systemically, to the whole of the infected part, and that there is no dead tissue remaining to form a nidus for the infection.

If there is no diminution of bacterial growth within a week, consideration must be given to the advisability of aspiration or surgical interference in order to gain better access to localised lesions.

The blood count is also of value in assessing the arrest of infection. A steady fall of the leucocyte count to within normal limits and a rise in the erythrocyte count are indications that good progress is being made.

(b) *Local infections.* In local lesions the subsidence of pain, redness, swelling and induration, the disappearance of pus, and the return of function, are all indications of progress. It must always be remembered that, apart from the relief of pain following incision and the local application of penicillin, there is little that is dramatic in the course of recovery from the infection. Treatment may be stopped within 5 days in acute conditions, but should often be continued for as long as 3 to 4 weeks in well established infections where there is much dead tissue to be absorbed. The final result will depend in such cases on continuing the treatment with penicillin until the bacteriological evidence indicates that infection has been arrested.

[B.M.B. 202]

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## PENICILLIN, A POPULAR TALK

*By Dr C. M. FLETCHER*

The discovery of the sulphonamide drugs, about which you heard last week, and which have brought about a revolution in medicine, was the result of the patient and methodical trial of one substance of known chemical composition after another until at last one with an inhibitory effect upon bacterial infections was found. Scientific advances are usually made along such planned, deliberate lines, but this is not always so. Sometimes blind chance opens a door to discovery and the keen observer is quick to seize the opportunity offered. It was blind chance that led to the discovery of penicillin, which is proving itself to be the safest and most powerful drug yet known in the treatment of infections by bacteria or germs.

In 1929, Professor Fleming, the bacteriologist at St Mary's Hospital in London, was growing a bacterium called a staphylococcus in an artificial culture medium (this is the bacterium that causes boils, carbuncles, chronic bone infections, and sometimes fatal blood poisoning). He had a layer of nutrient jelly in a shallow dish and on the surface of this jelly he had placed the bacteria to grow and multiply. He had meant to exclude all other germs, but he failed. Just as a housewife, making jam, may find that into one jar a spore of mildew has settled and begun to grow, forming a white furry mass on the surface of the jam, so onto one of Professor Fleming's plates of jelly a mould settled and began to grow. Such a contamination by a mould is not an uncommon accident in bacteriological work and is responsible for much wasted time. A less observant man than Fleming would have thrown the culture away without further ado, but in this particular case he noticed a curious thing. Around that part of the jelly on which the mould had grown, the staphylococcus had failed to grow. Usually bacteria and moulds will thrive together, but in this case they did not. There appeared to be something in the mould, or produced by the mould, which either killed the staphylococcus or at least stopped its growth.

Professor Fleming was quick to see the possible importance of this observation. He took a sample of the mould and set it to grow in some nutrient broth. He then examined the broth in which the mould had grown to see if it could prevent the growth of a staphylococcus. The experiment succeeded. The mould had produced in the broth some substance which could prevent the growth of not only the staphylococcus but also that of many other bacteria which cause disease. The mould proved to be a well known one called *penicillium notatum* and so Professor Fleming called the substance it produced penicillin. He suggested two uses for it. The first arose from the further discovery that some bacteria were unaffected by it, so that if penicillin was added to a mixture of various bacteria, only those unaffected would survive. Thus it could be used for separating out certain bacteria from a mixed culture. This use soon came to be quite frequently adopted by bacteriologists. Secondly he suggested its possible use for the control of bacterial infections in man, but this

suggestion could not be carried out, for it proved exceedingly difficult to isolate penicillin from various other substances in the broth in which the mould had grown, and trial injections into mice showed that some of these substances were poisonous. Thus the use of penicillin in man was considered to be impracticable. At that time the treatment of bacterial infections by chemical substances capable of preventing bacterial growth was not considered possible at all, and so no further attempts to use penicillin in this way were made until years later when the discovery of the sulphonamides revived interest in the subject.

Three years ago, in 1940, Professor Florey, and Dr Chain at Oxford turned their minds to penicillin, and determined to try to isolate and purify it, and see whether it might not be possible to use it for treating bacterial infections in man. Many difficult problems had to be overcome to achieve this end. To their solution they brought a team of chemists, bacteriologists, experimental workers and clinicians.

The first problem, that of growing the mould on a larger scale seemed easy at first, but soon difficulties arose. Although it was easily persuaded to grow in a mixture of salts and sugar in water, it would often refuse to produce any penicillin. This was partly explained by the discovery that some of the bacteria which are not affected by penicillin have the power of destroying it, so that if the broth became infected by any of these bacteria then the penicillin was destroyed as fast as the mould produced it. Thus it became necessary to grow the mould under strict precautions to exclude any bacteria from the air or from dust. Further it was found that very large quantities of mould had to be grown to produce adequate amounts of penicillin (about 200 pints of broth were required to produce enough to treat one case for one day). Eventually these difficulties were partly overcome and a whole room was turned into an incubator in which special culturing bottles were stacked to grow the mould. Meanwhile, the chemists were working on methods for extracting the penicillin from the broth and for purifying it, and eventually a large and complicated apparatus was designed which automatically carried out the extraction process. At last, after a year of hard work, the first specimens of penicillin in an almost pure state were obtained. It proved to be a yellow powder which dissolved very readily in water, had a bitter taste and a faint musty smell.

Now that almost pure penicillin had become available it was possible to investigate more fully its effect on various bacteria in artificial culture and to compare it with the sulphonamides. Under these conditions it was found to be at least 50 times more powerful than any sulphonamide, and to attack a rather wider range of bacteria. In particular its activity against the staphylococcus, which is usually only slightly effected by the sulphonamides, was its most promising property. Further advantages lay in its great solubility, its ease of diffusion, the fact that, unlike the sulphonamides, its activity was not diminished by the presence of pus, and the fact

that it was less harmful to living cells in tissue culture and to white blood cells than are the sulphonamides. One disadvantage was that it was easily destroyed by acid. This meant that it would be destroyed by the acid in the stomach. Injections would therefore be necessary in using it for the treatment of infections.

Encouraged by these findings, Professor Florey started to try the effect of penicillin on experimental infections in mice. These trials were equally encouraging. Many experiments were done of which the following is an example. 48 mice were injected with a fatal dose of a staphylococcus and 24 of them were given injections of penicillin every three hours for two days. All the treated mice survived and appeared none the worse, whereas all the untreated mice died within 24 hours. To make sure that penicillin had no poisonous effect, several mice were given doses many more times than was needed to cure infection, but they were quite unharmed.

The time had now arrived to make the first trial on a patient. A carefully purified specimen was tested several times on mice and then injected into a patient's vein. There was no serious effect, but the patient had a slight rise of temperature. The chemists applied a further process of purification to the drug and another dose was given to the patient. This time there was no ill effect at all. After several further trials of test doses, five cases of sepsis were chosen to be treated. These cases were all infected by bacteria on which the sulphonamides had had no effect. They received injections of penicillin every two or three hours by day and night for a period of one to three weeks. In all of them penicillin controlled the infection though two of them received too small a dose and the infection was only temporarily benefitted. These clinical trials gave important information. They showed that penicillin was as powerful in controlling infection in man as it had been in preventing the growth of bacteria in a laboratory, and they showed that penicillin was quite harmless to man. None of the patients who had received the drug suffered any of the unpleasant and even dangerous effects to which the sulphonamides may give rise.

All the supplies of penicillin used in these experiments and clinical trials were made by the chemists and their technicians in two or three rooms in one laboratory. They could not possibly produce enough for the wider trials that were now required. The time was 1941 when Britain's resources were strained to the uttermost by her solitary struggle and by the blitz on her towns. No British chemical firm could undertake the intricate process of growing the mould to produce penicillin on a large scale. So Professor Florey and Dr Heatley (who was chiefly responsible for developing the technique of extraction of penicillin) flew over to America with some of the mould, and several American firms offered to try to make penicillin on a commercial scale. By the beginning of 1942 further supplies became available and further and more extensive clinical trials were made possible. All of them confirmed the early promise and many cases of advanced sepsis with blood-poisoning, meningitis, pneumonia and

osteomyelitis, which had failed to respond to sulphonamides, proved curable by penicillin. There is now little doubt that penicillin is an almost perfect chemotherapeutic drug. That is to say it appears quite harmless to man, but most harmful to a wide variety of bacteria that cause disease.

You may wonder why it is not more widely used. The answer is that at present production is derived solely from culture of the mould, and this remains a very difficult process. The small available supplies are being devoted both in this country and in America to research and to the treatment of severe cases of sepsis resulting from war injury.

What hope is there then of penicillin ever becoming more widely available? There is good hope, but it may take a long time to be realised. For large scale production it will be essential to be able to make penicillin artificially by chemical methods. This was realised by the Oxford workers as soon as the difficulty of its preparation became apparent, and the chemists there set to work on the problem. The first step was to discover what the exact chemical constitution of penicillin might be. It was soon found that the molecule of penicillin is not a very large one—not much larger than that of some of the sulphonamide compounds—and so good hopes were entertained that its precise constitution would easily be found. This has, however, proved to be a most difficult problem and, up to the present time, it has not been solved, although some progress has been made. There is little doubt that sooner or later the problem will be solved and then it should be possible to produce penicillin artificially on a large scale. When that is done this invaluable drug will become available to everyone, but at present it is not available at all.

This is as far as the story of penicillin can be told. It is a story of a triumph of keen observation, and close co-operation between scientists with various specialised abilities. But the story is not finished. Many exciting possibilities remain. When the chemical constitution of penicillin has been established, compounds similar to it, but with a wider range of activity may be synthesised, just as well all the various sulphonamides have been developed from the original discovery of sulphanilamide. Again, if one mould can produce penicillin, perhaps other moulds will produce other substances with equally valuable medicinal properties. This possibility is now being explored and is showing promise. If bacteria could think, they would have good reason to fear what the future may bring.

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(A BBC Talk, supplied by the BBC, New Delhi)



# Book Reviews and Notices

## CLINICAL DIAGNOSIS BY LABORATORY EXAMINATIONS

By JOHN A. KOLMER, M.S., M.D., DR. P.H., S.C.D., LL.D., L.H.D., F.A.C.P. Professor of Medicine in the School of Medicine and the School of Dentistry of the Temple University; Director of the Research Institute of Cutaneous Medicine, formerly Professor of Pathology and Bacteriology in the Graduate School of Medicine of the University of Pennsylvania. First Edition. Price \$8.00 Pp 1270 (XXXII contents, 1107 reading and 131 Index) 179 Illustrations and 187 Summary Diagnostic Tables. New York and London, D. Appleton Century Company, 1948

The preparation of this new book was undertaken by Dr. Kolmer to meet the growing necessity for adequately teaching clinical pathology to medical students. A single volume that would present fully and clearly the clinical interpretations of laboratory examinations and their practical applications in the diagnosis of disease, and would at the same time, give such laboratory technical methods as would suffice for their purpose, was badly needed and it is a pleasure to be able to say that Dr. Kolmer has amply succeeded in his effort. It is generally recognised that responsibility lies heavy, not on the teachers and specialist practitioners of clinical pathology alone, but also, to a fairly appreciable extent, on the general practitioners and consultants who are expected to know exactly what kinds of, and how properly to collect, requisite materials and samples from the patient for the different laboratory investigations. Keeping this in mind, the author has described in detail the appropriate methods and procedures for collecting samples in different diseases and also the proper preparation of the patient preliminary to such collection. We feel that this book will be of very great help not only to the teacher and the student, but also to the practitioner who would wish to feel sure of his ground.

The book is divided into three parts. Part one deals with Clinical interpretation of laboratory examinations, Part Two deals with Practical application of laboratory examinations in Clinical diagnosis and Part Three deals with Technic of Laboratory examinations. We can say with confidence that with the help of an exhaustive Index of 131 pages, the reader will easily find ample references to any subject he may wish to look up.

The words "Clinical Diagnosis" were formerly generally used to mean a diagnosis made "at the bed-side" basing the conclusion upon the history of the disease including symptoms and the signs elicited by the physical examination alone. But nowadays such a narrow meaning would not do, and the words "clinical diagnosis" are being used in their wider sense to include the findings of the various laboratory investigations that are usually carried out as very necessary routine examinations, such as, blood-counts, urine examinations, Wassermann and agglutination tests, bio-chemical estimations and bacteriological examinations. It is thus apparent that a good working knowledge of clinical pathology as is given in this book is essential not only for the student but also for the modern practitioner in

order that he may be able to diagnose and treat his cases on approved scientific lines

The past thirty or forty years have been extraordinarily fruitful in the advancement of our knowledge of biochemistry, bacteriology, parasitology, immunology, and allied subjects. There have been evolved also a large number of new and improved methods of laboratory examinations of great practical value in the diagnosis of disease. And yet, even in these days, it is not rare to meet with 'practitioners' who would far rather depend upon histories, physical examination and their "instinctive feelings" to arrive at a diagnosis than to take the available help of laboratory investigations. But there can be no excuse for such an attitude. Every medical man who keeps himself abreast of the recent advances in laboratory examinations, cannot but be convinced that a judicious combination of the "art of medicine" as exemplified by the physical examination and the "science of medicine" as exemplified by the laboratory investigations, is of the utmost importance in the interests of both the patient and the practitioner, and it is essential that the medical man should be equipped with such necessary knowledge of scientific investigations as is given in Dr Kolmer's "Clinical Diagnosis"

Pathology is and must remain the sure foundation on which alone the imposing structure of Medicine can be built, and dealing with problems affecting the living body a new kind of pathologist has been brought into existence. He is called the "Clinical Pathologist". It is he who is expected to be not only an experienced Laboratory technologist, but also to possess a sound special knowledge of the abnormal changes occurring in the body during life and expertly to interpret and appraise the laboratory findings in relation to the diagnosis of disease. It is the purpose of the author to put all the relevant information given in an easily accessible form in this One-Volume-Book at the disposal not only of the teacher and the student, but also of every practising physician and surgeon, so that if he cares to avail himself of it, he may become, in a broad though of course limited sense, his own "Clinical Pathologist" in so far as the interpretation of laboratory examinations is concerned.

We have no doubt that Dr Kolmer has succeeded in placing a very good and entirely satisfactory book on Clinical Diagnosis before the medical profession and we feel that every medical man will be all the better for having it in his library for everyday reference.

S. K. V

**SULFANILAMIDE, SULFAPYRINIDE AND ALLIED COMPOUNDS  
IN INFECTIONS** By Maurice A. Schnitker, M.D. Cloth Price 8 sh  
6d Pp 72 New York and London Oxford University Press, 1940

The sulpha group of drugs, recently introduced to the therapeutic armamentarium of the practising physician, has wide applications in clinical practice and it is essential for the practitioner to be fully acquainted with the mode of action, methods of administration and dosage, therapeutic efficacy and toxic results of the chief members

of the group offered to him by manufacturers under different trade names. The literature on the subject since Domagk announced the effectiveness of prontosil in preventing death in experimental streptococcal infections in mice, in February, 1935, has been enormous and daily increasing and the opinions expressed often conflicting. The bewildered practitioner is in dire need of a brief authoritative summary of the established scientific facts about the action of these drugs and a critical evaluation of the therapeutic claims in their favour. Such a presentation, we believe, is this small monograph, reprinted from Oxford Loose-Leaf Medicine, for the use of general practitioners. It shows briefly and clearly how and when to use these new preparations and what to expect from them. A lot of new material has accumulated since this review was printed (1940), but the student can use this as a basis to add on the newer knowledge. We entirely agree with Dr Henry A Christian, who has written a foreword to the book, that the book is authoritative, inclusive and comprehensive, and up-to-date as far as possible, and will prove a great help to doctors in their daily problems in the management of infections and infectious diseases.

L. I. I

## Announcement

Shree Gulab Kunverba Ayurveda Association of Jamnagar requests us to announce that its Aurveda Publication Department has planned to issue an elucidative and illustrative edition of CHARAKA SAMHITA, in six volumes. The text will be in original Sanskrit, Hindi and English, with critical notes and exhaustive glossaries. Prepublication price, de luxe edition Rs 100/-/-, ordinary edition Rs 6/-/- per set. 25% advance to be sent with the order.

The Indo-Pharma Pharmaceutical Works, Bombay inform us that

- (1) VITAMINDON C (Vitamin C) is available again, in packings of 30 and 100—in any quantity—from all good chemists or directly from their office, and
- (2) they have put three new preparations on the market recently, viz YEASTINDON (Medicinal Yeast tablets), DICALCINDON "D" (Dicalcium Phosphate cum Vitamin D), and NICAMIDINDON (NICOTINIC ACID AMIDE Tablets).

# The Indian Physician

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VOL III NO 5

MAY, 1944

WHOLE NO 29

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## Original Contributions

### CONTINUOUS SPINAL ANESTHESIA

*By*

Dr B N SIRCAR

M. B. B S. D A (ENG)

Anesthetist, Tata Memorial Hospital Bombay

I am going to speak to you on continuous spinal anesthesia but before I begin the subject, I must express my thanks to the members of the Committee for giving me this opportunity of speaking on a subject like anesthesia which so far has not received much attention from the surgical profession. Antisepsis and later asepsis, together with anesthesia made possible the development of modern surgery. Many years ago the requirements of anesthesia were simple, the relief of pain while surgical manipulations were carried out was probably the only desideratum. But to-day with the great advances in surgical technic and with the more ambitious nature of operations attempted by surgeons, the methods of anesthesia which seemed adequate formerly are definitely found inadequate for many of the modern operative procedures. This demand has introduced many new drugs, methods and technics which can only be administered by specially trained anesthetists.

Continuous spinal anesthesia is one of the recent developments in anesthesia. Though spinal anesthesia has not found much favour in the work at the Tata Memorial Hospital, it was decided to try continuous spinal anesthesia with an idea to studying the method and its uses. This paper is based on a study of 20 cases in which this type of anesthesia was administered recently in our hospital in the last six months. It is too early to base any definite opinion on 20 cases but as this method

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A paper read before the 2nd Bombay Medical Congress at C J Hall, Bombay, on Feb 21, 1944

has worked quite satisfactorily in our hands, I have decided to give you an idea of the technic used

Spinal anesthesia has undergone many improvements since its discovery by Corning (1885) and its introduction into clinical medicine by Bier (1899). Modern interest was revived by the discovery of ephedrine by Chen and Schmidt and its use to combat the fall of blood pressure during spinal analgesia by Ocherbald and Dillon. However, even with a relatively non-toxic agent like novocain and adequate vasoconstrictor—ephedrine—there was much to be desired clinically in spinal anesthesia. Satisfactory height and duration of anesthesia were difficult and sometimes impossible to obtain by a single injection of a previously determined dose of the spinal anesthetic agent. Consequently many new spinal anesthetic agents, *i.e.* spinocaine, metycaine, pantocaine and percaïne and various methods of administering them were introduced in an attempt to increase the controllability and the duration of anesthesia. All the same the problem of spinal anesthesia remained—its failure to produce analgesia and its wearing off sooner than expected if the operation took more time than was anticipated.

William T. Lemmon of Philadelphia has provided the most recent advance in this field with his introduction of continuous spinal anesthesia—a method of producing prolonged analgesia by injecting the anesthetic agent in fractional doses as needed during the operation. Various anesthetic agents, *i.e.* procaine, nupercaine, metycaine and pantocaine have been used by various workers. However, novocain seems to be particularly well suited to this method of administration because of its lack of toxicity, the rapid onset of analgesia and the relatively short duration of action. Various strengths ranging from 3 to 10% of novocain solution have been used by different workers, but recently Fraser (1943) has published a series of cases using 1% novocain solution in saline with satisfactory result. Whenever a new technic is to be used it is safer to use the weakest effective solution, hence it was decided to use 1% novocain solution as suggested by Fraser. It has given excellent result in our cases also.

**Equipment** In order to administer continuous spinal anesthesia special equipment is necessary. This consists of a special mattress so designed that the spinal needle may remain in place during the operation (Fig 1 A). This mattress is 5

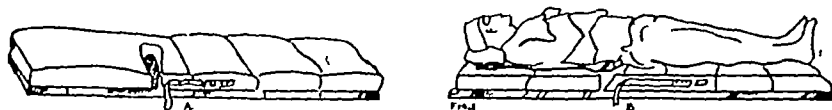


Fig 1 A and B

inches thick, 18 inches wide and approximately 6 feet long. It is made up of two sections, the upper section accommodates the trunk of the body while the lower section takes care of the lower extremities, the two sections being detachable. The upper part has a cut-out portion to accommodate the needle in the lumbar spine when the patient is in supine position. The break between the two sections of the mattress allows the lower section to be removed for perineal operations and to be replaced after pulling the patient to the head-end of the operation table (Fig 2).

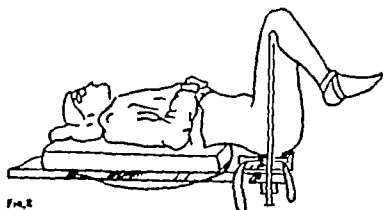


Fig 2

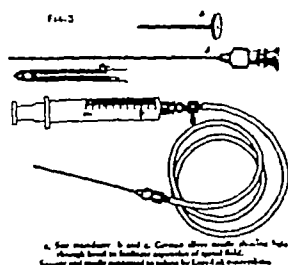


Fig 3

In America special malleable spinal needles of German-silver either of 18 or 19 gauge, are being used. The idea of using a malleable needle is that it will not snap because of its flexibility. It has also a small hole in the bevel to facilitate aspiration of spinal fluid when the barbotage method is being used or to withdraw the spinal fluid when toxic symptoms appear early to decrease rapidly the concentration of the anesthetic drug. We have used unhardened stainless steel Barker B D needle 18 gauge without any misadventure so far. On two occasions the needle was found to be bent on withdrawal but there have been no breakages. The lumbar puncture needle remains projecting from the back and is connected with a syringe containing analgesic solution by means of 30 inch of thick-walled fine-bore rubber tubing. A tap near syringe prevents csf from flowing back into it, and can be turned on when additional doses are needed (Fig 3).

*Technic* —The technic begins with pre-operative sedation, the pre-anesthetic medication used in our clinic has been as follows —on the morning of operation a dose of barbiturate (i.e., nembutal gr  $\frac{1}{2}$  to gr 1) is given two hours before operation, followed half an hour later by an injection of morphine and atropine in the ratio of 25 to 1 (i.e. morphia gr  $\frac{1}{4}$  and atropine gr 1/100) depending on individual patients

In all cases the patient is placed in the left lateral position for the lumbar puncture in such a way that the selected interspace corresponds with the gap in the mattress. For upper abdominal work the second interspace is used, for mid-abdominal operations the third interspace, while for lower abdominal and perineal procedures the fourth interspace is selected. The back is cleaned, draped and a skin wheal is raised with novocain at the site of lumbar puncture. Ephedrine gr  $\frac{3}{4}$  is injected as a routine through the anesthetised skin. The skin is then punctured with the Sise introducer which is twisted around to make a passageway for the lumbar puncture needle and then withdrawn. The spinal puncture is made through the passageway made by the introducer and when free fluid is obtained the initial calculated dose is injected. The lumbar puncture needle is then connected with the already filled syringe and tubing containing the anesthetic solution. When this is done the patient is turned gently in the supine position so that the needle rests in the centre of the gap in the mattress without touching the table or mattress any time. The syringe is taped to the mattress at the right side of the patient's head (Fig 1 B). Additional doses of solution can be then injected as required.

For lower abdominal operations the table remains level, while for upper abdominal operations a 5° Trendelenburg tilt is required with the head well-flexed on a pillow to prevent the solution from going higher than 4th or 5th thoracic segment.

*Dosages* —The initial dose is 1 mgm of novocain for each lb of body weight, taking into consideration the build and general condition of the patient and the height of the analgesia required. We have used the initial doses as follows —

Upper abdomen	140 to 150 mgm of novocain
Mid-abdomen	100 to 120 mgm of novocain
Lower abdomen	80 to 100 mgm of novocain

The final consideration is the question of supplementary fractional doses. Investigative studies of Heinbaker have

demonstrated that it requires smaller amount of any drug to maintain spinal anesthesia than to induce spinal anesthesia. The three prominent signs of the wearing off of anesthesia are (1) the patient first complains of discomfort and then pain, (2) abdominal muscles grow tense, and (3) the dilatation of the previously contracted gut.

Workers using higher concentration of novocain advise the addition of the first supplementary dose after an hour, but on using 1% novocain it was noticed by us that the patient complained of discomfort after 30 minutes. Hence the first supplementary dose of 30 to 40 mgm was added after 20-25 minutes in our series.

*Selection of cases*—Every case was selected on the basis of the patient's ability to withstand an operation under spinal anesthesia. Cases were selected in which the length of the operative period could not be previously determined and those entailed difficult surgical procedures such as gastric resections, large bowel resections and hysterectomies.

Table I shows the 20 cases done in our hospital with the continuous spinal anesthesia. It also shows the duration of the operative procedure and the amount of novocain used.

TABLE I

No. of cases	Operative procedure	Average time of operation	Average dose of Novocain used
6	Subtotal Gastric Resection and Entero enterostomy	3 hrs 50 mins	500 mgm
1	Exploratory Laparotomy (Upper abdomen)	1 hr 50 mins	200 mgm.
1	Exploratory Laparotomy and appendicectomy	1 hr 30 mins	210 mgm
2	Ileo-transverse colostomy	2 hrs 30 mins	250 mgm
1	Exploratory Laparotomy and colostomy	40 mins	150 mgm
1	II Stage Colectomy	2 hrs 30 mins	250 mgm
1	I Stage Lahey for cancer rectum	2 hrs 10 mins	250 mgm
	Total Hysterectomy	2 hrs 10 mins	230 mgm
2	Panhysterectomy	2 hrs 20 mins	275 mgm
1	Subtotal Hysterectomy	2 hrs 45 mins	300 mgm
2	Vaginal Hysterectomy	2 hrs 10 mins	240 mgm

It is our routine to maintain a complete anesthetic chart (Fig 4) on all cases and these cases form no exception. Blood pressure, pulse, respiration, the height of anesthesia and even the height of anesthesia reached with every supplementary dose have been charted. Intelligent patients could always tell the level of anesthesia when tested with a pin. In one case of hysterectomy under high Trendelenburg position the level of anesthesia used to change from T<sub>8</sub> to T<sub>9</sub> with each supplementary dose.

### Observations

(1) No technical difficulties were encountered either to reach the proper level of anesthesia or to maintain it till the end of operation. The needle remained in position in all cases but withdrawal of fluid was not possible in 80% of our cases.



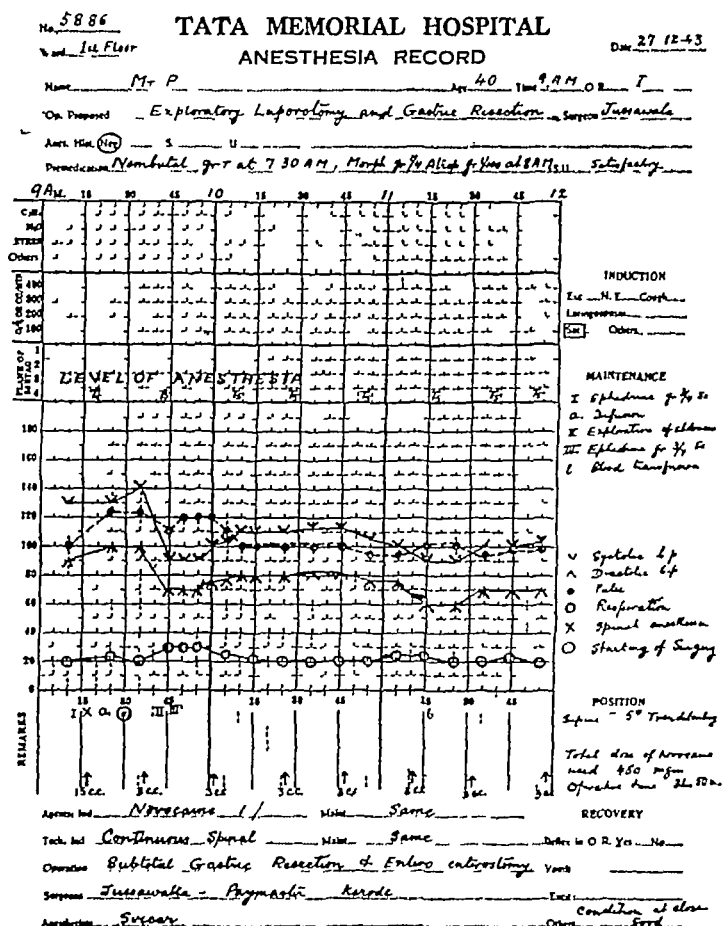


Fig 4—shows the anesthetic chart of a case of subtotal gastric resection with entero-enterostomy done under continuous spinal anesthesia

because of inability to obtain the special needles recommended for this purpose. Withdrawal of fluid is recommended when the patient shows signs of toxicity to the anesthetic drug and also after the operation to shorten the anesthetic period. Muscular relaxation was perfect and there was no difficulty in closing the peritoneum in any case.

(2) Blood pressure readings showed less variations than in the case of single-injection spinal anesthesia. In all these cases 5% glucose-saline was given routinely by placing an intravenous drip in the great saphenous vein where it ascends in front of the tibial malleolus. Blood transfusion has also been given whenever needed during the operation. In two cases

there was a considerable drop in blood pressure during traction on the stomach. Although the same changes in circulation often occur during inhalation anesthesia from traction, it seemed that the changes were much more pronounced during spinal anesthesia.

(3) Respiratory embarrassment was not noticed in any of the cases though the level of anesthesia reached to T<sub>3</sub> in one case. Oxygen was given by mask and bag as a supportive measure in that case.

(4) Post-operative pulmonary complications—In this series we had two cases of collapse of base of the right lung and one case of acute bronchitis in a patient who had a history of chronic bronchitis for years. When compared with a similar series of abdominal operations done with inhalation anesthesia in our clinic, the percentage of pulmonary complications compares equally well with the cases done under continuous spinal anesthesia. Other workers believe that post-operative complications were slightly reduced by this technique.

(5) The problem of epigastric or substernal pain with retching, vomiting or hiccoughs in the course of upper abdominal operations under spinal anesthesia remains to be solved. Two of our upper abdominal cases had retching and hiccough when traction was made on the stomach. Intravenous atropine has been recommended to stop the hiccoughs. Exponents of spinal anesthesia advocate the use of cyclopropane or intravenous anesthesia to prevent these disturbances. In one of our cases of hysterectomy the patient had to be put to sleep with cyclopropane as the patient had terrific pain and retching on pulling on the uterus. We are of opinion that this complementary anesthesia leads to increased danger of post-operative pulmonary complications.

(6) Headaches have been infrequent as compared to one single injection spinal. Six cases complained of slight headache which disappeared within 24 hours.

Among other neurological complications a case of sciatica has been reported from the Lahey clinic.

(7) Retention—6 cases had retention of urine, 4 of them for 12 hours, one case for 20 hours and the other for 30 hours. Cases have been reported where the retention has lasted as long as 15 days after continuous spinal anesthesia.

## SUMMARY AND COMMENT

The technic of continuous spinal anesthesia with a review of our 20 cases has been described. A more extensive use of this method will be necessary before an opinion can be formed concerning the proper choice of the patient for this method. The advantage of this method lies in the fact that it allows the surgeons unlimited operating time with excellent muscular relaxation. It does not solve the other problems inherent in the administration of spinal anesthesia.

## DISCUSSION BY DR E J BORGES

If one must judge an anesthetic, one must consider how far it answers three questions: (1) How safe is it for the patient, (2) how easy is it for the anesthetist to administer, (3) how much comfort and ease in the operative procedure it affords to the surgeon.

Dr Sircar has already dealt with the first two criteria and I shall only restrict myself to considering how far continuous spinal anesthesia answers the third question.

Continuous spinal anesthesia has all the advantages of ordinary spinal anesthesia. It gives excellent relaxation of the abdominal wall, the intestines simply fall away from the operative field and all manipulations and access to organs are very much simplified. But it scores over ordinary spinal anesthesia in at least two points. First of all, when ordinary spinal anesthesia is administered, the effect begins to wear off in from 45 minutes to 2½ hours and at the end of this period some other form of anesthesia has to be resorted to if the operation is not to end in a free fight between the patient and the surgeon. Continuous spinal anesthesia does away with this annoyance and interruption. Secondly, it also does away with haste from the anxiety of the surgeon to finish the operation before the anesthesia wears off, and you will all agree that haste is not conducive to good surgery, particularly in lengthy and difficult procedures which are the best indication for continuous spinal anesthesia. In a gastric resection, for instance, it is very important to invert and protect the duodenal stump very carefully. A hasty technique here may be responsible for a leak with disastrous results.

But continuous spinal anesthesia also has the disadvantages of ordinary spinal anesthesia and of these I have time to mention only one and that is the discomfort that is always

caused to the patient during pulling and tugging procedures. In one of our patients there was severe retching during a gastric resection and in another there was hiccough.

However, when all is considered, if I am given the choice between continuous spinal anesthesia and inhalation anesthesia administered by an expert anesthetist as we are accustomed to at our hospital, I would always prefer inhalation anesthesia.

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(Continued from page 192) REMARKS—by Dr K. P. MODY

field also gave excellent results under x-ray treatment, so much so that treatment apparatus was already manufactured of a portable type so that treatment could be given within 24 hours. Acute sinusitis, acute sub-deltoid bursitis, and acute post-operative parotitis were also greatly benefitted, as also certain types of pneumonia.

Referring to new technical developments he mentioned a newly introduced method for x-ray examination of the lungs, so important in the detection of early tubercle, known as photo-roentgenography or photo-fluorography. In this method the image on the x-ray screen was photographed by a special camera attachment on a small film, 4 by 5 inches or smaller still on a 35 mm film. The great advantage of this method is its cheapness and economy. After the war it was expected there would be a great increase in the incidence of tuberculosis, by this inexpensive method large sections of the public could be radiographed cheaply and efficiently, hence the expression "mass radiography" came to be applied.

Revolutionary changes had taken place in deep therapy instruments. Already one million and two million volt machines were in actual operation at many clinics. In this connection Dr Mody warned the lay public and the medical profession against thinking that because these supervoltage machines were available the results were bound to be better in the treatment of cancer. That was not so and will never be so. It is true, however, that these machines were very convenient in the treatment of deep seated neoplasms. Evan 3 and 5 million volt machines were constructed, but they were in the experimental stage. These megavoltage machines were used not directly on the patients, but they were utilised to break up the atom with the liberation of the centre part of the atom, known as the neutron. The patient was treated by these liberated neutrons, which were said to be more cancericidal than x-rays. He then referred briefly to artificial radio-activity and their use in leukaemias and lympho-sarcomas. This was still in the experimental stage, and time alone would show their value.

# THE VENEREAL DISEASES

By

Lt. Col E E PREBBLE

R. A. M. C., *Adviser in Venereology, India Command*

I hope to place before you today a paper bearing on the venereal diseases. Much that I say will doubtless be quite new to you because it represents my personal beliefs based on the clinical and bacteriological experience of fifteen years' work. There must be few diseases where such a perfect liaison exists between the clinic and the laboratory and where the diagnosis, treatment and prognosis can be so accurately established from bacteriological findings. Moreover, upon their efficient treatment depends the happiness not only of the individual but of the family and perhaps succeeding generations.

We have then the *treponema pallidum*, an animal organism—the cause of syphilis, whose activities are entirely concerned with endarteritis and peri-arteritis, the gonococcus, a vegetable coccus whose typical effect is a purulent catarrh, the bacillus of Ducrey, a vegetable bacillus, whose effects are upon the skin and the regional lymphatic glands, the filterable virus of lymphopathia venerea or climatic bubo which produces necrosis of glands and stricture of the rectum in humans and meningo-encephalitis in mice, and the Donovan body which causes locally malignant ulceration of the genital and perigenital area. All are parasites depending for their continued existence on a living host and more particularly a human host.

Syphilis is not frequently transmitted from one person to another during the active eruptive phases of the primary and secondary stages of the disease, but is derived from the natural secretions of the infected person. The most commonly involved secretions are the seminal fluid of the male, the mucus discharges from cervix and uterus in the female, the saliva and the milk of the nursing mother. An example of seminal infection is shown in the following case.

A doctor performing a circumcision on an infected patient sustained a prick from a needle. Some weeks later his child was discovered to be suffering from syphilis. An investigation revealed a cervical chancre in the wife and shortly afterwards the doctor himself developed signs of secondary syphilis. Here therefore we have a case of seminal infection of the wife before any active signs of disease had developed in the husband and in addition an infection of the child through the milk of the mother.

I believe that seminal transmission may occur up to five years after infection and that after this period the male is no longer infectious to the female. In the case of women the period of infectivity

to the male is, as a rule, shorter and probably is not prolonged for more than two years. It must be remembered, however, that the woman is always a potent source of infection to her unborn child, no matter how long a period has elapsed between infection and conception. I think it unwise for a man to beget children or expose his wife to infection for five years after contracting syphilis in spite of repeated negative blood tests. In the case of the woman, the occurrence of pregnancy at any date after syphilis has been contracted and, in spite of repeated negative blood tests, calls for energetic treatment throughout the pregnancy if a healthy child is desired. Further a woman who contracts syphilis after the sixth month of pregnancy may not infect her child in utero but the infection may be conveyed by the milk to the child after birth.

The diagnosis of syphilis should not lightly be made, the treatment is long and tedious and sometimes fraught with danger. Any case of genital ulceration should be carefully examined, all should be considered as possibly syphilitic until definitely disproved. All such cases should have at least three dark ground examinations, the sore meanwhile being dressed with saline only. A blood test should be performed as soon as possible. If the dark ground tests are all negative local antiseptics may then be applied. Blood tests should be performed at monthly intervals until 4 months after the appearance of the sore. If all are negative, syphilis has been definitely excluded. The specific test for Chancroid is called the Ito-Reenstierna test and it consists in injecting 100 million dead bacilli of Ducrey in 0.2 cc of saline endodermally in the suspected case. A positive reaction is marked by inflammation and papulation at the site of the injection within 48 hours, and proves the presence of chancroidal element in the ulcer, but it does not disprove the possible presence of syphilis.

The Wassermann test still holds place of pride in the diagnosis of syphilis in spite of a crop of more modern tests which depend upon precipitation or flocculation in the presence of syphilitic serum. It has to be remembered, however, that the Wassermann may not become positive for four months after inoculation with syphilis and that after the third year of the disease the reaction tends to become inconstant and may even remain negative in the face of active visceral lesions of syphilis. A negative Wassermann of itself does not mean "cure" nor freedom from infection. A case illustrating the negative phase found in early and late syphilis was that of a man who attended a clinic in 1922 suffering from a small and apparently "soft" sore. No examination for treponemata was done, but a blood Wassermann proved negative. The sore soon healed and in 1923 the patient married. In 1925 a child was born suffering from congenital syphilis. Husband, wife and child were found to have positive Wassermann tests and came under treatment. The husband's blood became negative, and he absconded from treatment. In 1930, he returned with severe gummatous ulceration of both legs, but repeated Wassermann test failed to show positive reactions. Such cases are not rare and I am sure you have all seen cases of clinical *tabes dorsalis* where both blood and cerebro-spinal fluid tests proved completely negative. Obviously then

in late syphilis, clinical judgment is of more value than laboratory tests

The treatment of gonorrhoea has, in the past few years, come much into prominence in the contemporary medical weeklies. The discovery of prontosil by Domagk led to its use in the treatment of many bacterial diseases and gonorrhoea was early exploited. Later we have seen the introduction of other members of the group. The most commonly used in this country is a sulphapyridine or M & B 693, although if adequate supplies were available even better results would be obtained with sulphathiazole and best of all with sulphadiazine. The immediate effects of these drugs in sufficient dosage is little short of magical in the average case of gonorrhoea. Discharge ceases and the urine becomes free of pus in two or three days, complications seldom develop and established complications usually respond rapidly. An illustrative case is that of a patient with an acute posterior urethritis and trigonitis, who had terminal haematuria and severe pain on micturition, with strangury and frequency. The prognosis in such a case used to be grave and uncertain and treatment could only be by sedatives, sandalwood oil, hyoscymus and potassium citrate. Bladder lavage could not possibly be given for many days and even then it was fraught with dire consequences such as the development of epididymitis. He was given M & B 693 in doses of two half gram tablets four times daily and ordered to drink copious amounts of fluid. Two days later all symptoms had gone and the urine was clear with a few pus shreds. It was a most dramatic achievement! However, like most new remedies in medicine we have now found that some cases do not respond to treatment with these drugs and we are thrown back on the older and well tried remedies. In order to be effective the sulphonamides must be administered according to a fixed plan, irregular treatment is responsible for chronic uncured cases and for so-called sulphonamide-fast cases. The sale of this potent and dangerous drug should be restricted except on the prescription of a medical practitioner. The present indiscriminate sale of the drug in the bazaar is directly responsible for much uncured gonorrhoea with a consequent spread of infection by people who believe themselves to be cured.

The treatment of early syphilis is one of the most efficient of all therapeutic methods, provided that one keeps the body flooded with arsenic and a heavy metal. Three short bursts of treatment of six weeks' duration are required in the case of sero-negative primary syphilis. In my experience, by far, the most satisfactory method of treatment consists of bi-weekly injections of arsenic and bismuth, a total of 45 gm of arsenic and 24 gm of bismuth constituting one course of treatment. The bismuth forms a depot at the site of injection and during the rest periods the patient is actually under continuous treatment by slow absorption from this depot. Rest periods between courses of three months are recommended. In no case so treated will the Wassermann remain positive after one course of treatment followed by three months' rest. In no case where three such courses have been given has there been a clinical or serological relapse and no case so treated has shown a pathological cerebro-

spinal fluid in the fifth year of the disease or later. This leads one to a most important point in treatment, namely, that if a patient presents himself for treatment after the second year of his disease with a positive blood Wassermann, and especially if he has been irregularly treated, a lumbar puncture must be done before any arsenical treatment whatever is given. If the cerebro-spinal fluid is completely negative, trivalent arsenicals may be given, provided no contra-indication exists, but if the cerebro-spinal fluid is abnormal and suggestive of neuro-syphilis, pentavalent arsenicals are the choice. One cannot too frequently stress the necessity of regular well ordered and controlled therapy, irregular treatment is more dangerous than no treatment at all. The arsenical drug should always be administered by the intravenous route. Sulpharsphenamine is much more toxic and much less therapeutically effective than neo-arsphenamine and its use should be abandoned.

A great problem awaits you in India. No co-ordinated scheme exists for the adequate treatment of the civil population in this vast country. So-called treatment is given sporadically by medical men with little or no knowledge of these diseases and often, I fear, by non-medical men who are an even greater danger. Much requires to be done, clinics must be established worthy of the enormous work which awaits them, treatment must be taken out of the hands of inexperienced medical practitioners and unqualified quacks, the public must be educated to the dangers of the venereal diseases and to the necessity for expert treatment. The press and the radio must be employed to bring information to the masses but first of all you must have many first class clinics for the free treatment of the people. This is a vast public health problem but it must be faced and as soon as possible. Public opinion must be aroused to the realisation that the venereal diseases are diseases like any other diseases and they are preventable.

I hope that you will not consider my closing remarks outside my province. I am interested in all the problems of venereal diseases in whatever part of the world they occur. I have travelled widely through your country and am deeply conscious of what has to be done.



# SUBCONJUNCTIVAL INJECTIONS OF SOLUSEPTASIN IN OCULAR SEPSIS

by  
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AND  
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Although the number of cases on which the subject of this paper has been based is small and the observations comparatively brief, we feel that there are sufficient grounds for us to be optimistic about the form of therapy we practise for those dangerous maladies of the eye which may conveniently be grouped under one head—"Ocular Sepsis". Such a study of no more than 25 cases, extending over a period of no more than 6 months, must necessarily be void of those critical tests—the passage of time, and the value of numbers, and the advent of this conference, with the golden opportunity to give vent to our optimism may be considered the only excuse to rush with our observations and conclusions, which may otherwise seem premature.

Neither do we claim any originality in this form of treatment, as no doubt sulfonamide therapy orally and parentally has long been practised for the relief of ocular sepsis, and to change this to a subconjunctival method of approach to achieve the same end may only be considered an insult to any claim on originality. Our little paper is a faithful record of the cases so treated, our observations on the same, with suggestions of dosage etc., and the probable explanations of some of our failures.

The 25 cases on which this treatment was tried were of the following nature —

- 16 cases of hypopyon ulcer in various degrees of intensity
- 2 cases of post-operative sepsis
- 4 cases of suppurating enophthalmitis, of a nature that would have ordinarily required evisceration
- 1 case of Mooren's ulcer with hypopyon
- 1 case of neuroparalytic keratitis with hypopyon
- 1 case of trachomatous ulcer of the cornea

The *technique* that was used is simple. After instillation of 2 drops of 2 per cent pantocain in the conjunctival sac about 5 drops of 1 per cent novocain are injected subconjunctivally at the proposed site of injection. Then the soluseptasin solution of the required strength and quantity is injected at the same place. The site of injection is either deep in Tenon's capsule or just subconjunctival, and is changed from day to day.

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A paper read before the 2nd Bombay Medical Congress, at C.J. Hall, Bombay, Feb 21, 1944.

In the majority of cases no other form of special treatment for ocular sepsis like carbollisation, thermophore, ultra-violet therapy etc was employed

As regards the dosage the smallest dose we have tried is 1/30th of a grain and the largest 1-2/3 gr It would be easier to talk of the dosage by weight rather than by the quantity and strength of the sol injected For example 1 c c of a 5 per cent sol and (0.5 c c) of a 10 per cent solution have the same quantity of soluseptasin, viz 2/3rd grain, and it matters little which strength solution you inject

The dose is in the neighbourhood of 1 grain, 2/3rd gr to 1-1/3 gr being the usual range, depending directly upon the severity of the disease It is significant that when a dose as small as 1/30 gr was used, the hypopyon disappeared perhaps as readily as when larger doses were used, but we must confess that we have not had an opportunity yet of determining the minimum effective dose, as lately we have not had a sufficiently mild or early case to allow us the latitude to try out a smaller dose

#### INTERVAL AND NUMBER OF INJECTIONS

The injections are given daily, in almost all cases, except when such a feature like excessive pain, headache, or an objection on the part of the patient prevents us from doing so The majority of patients have no objection in tolerating a daily injection The number of injections varied from 2 to 20, weaker solutions requiring a longer course Generalising the subject of dosage, time-interval, and number of injections, we would say that a dose of 1 gr repeated daily for 10 days would be an average good dose

#### RESULTS

Coming to the results we shall first take those in *hypopyon keratitis* Here is a chart (shown at the meeting but not printed here) which will give you a comprehensive idea of the nature of our investigations and the results

First come the columns of age and the kind of patient, the degree of nutrition or malnutrition and the severity of the case The subsequent columns show successively the results of a smear and sac examination Then come the columns for dosage minimum and maximum, employed and the number of injections administered The results are shown in the succeeding columns, showing the number of day's treatment which brought about the subsidence and disappearance of pain, pus, and discharge The cures and failures, vision before and after the treatment in the next columns and the complications—perforation and recurrences in the last column, leaving remarks of interest to the very last

Looking at the chart we cannot help concluding that the relief of pain is the first good the injections render, which is done by the very first injection in many cases Then comes the subsidence of oedema and chemosis Hypopyon disappears almost as readily, and the subsidence of the posterior abscess follows on its heels The most annoying part of the ulcer is the centralmost part which remains resistant, but finally obliges by healing after consuming some five more injections

We believe the most important result to be noticed is the frequency with which perforation of ulcers can be prevented. And when these ulcers, which ordinarily perforate so readily, do actually perforate, the perforation is benign i.e. little iris tissue prolapses, and the ulcer heals with a firm cicatrix with little tendency to bulge.

The opacities left after healing are comparatively thinner with a consequent improvement in vision considerably better than one ordinarily expects after this ulcer. We have seen patients with reduction in vision to mere P. L. being restored to useful vision at the end.

The muco-purulent discharge that may be present gets reduced and disappears under the same treatment, no applications of silver nitrate or other antiseptics being quite necessary in most cases.

As regards the two cases of *post-operative sepsis* one improved to the extent that the eyeball was saved from enucleation, the other did not respond a jot to treatment. In both these cases no organisms could be found in the discharge. Both the cases may definitely be regarded as of exogenic infection because the first eye operated 10 days previous to the second, healed without any trouble at all. Although the result is 50% failure in the two cases, we feel that in subconjunctival injections of soluseptasin we have a supreme remedy for this most dreaded complication after intraocular operations.

Next, to talk of *suppurating enophthalmitis* of which we have treated four, they were cases where ordinarily one would have recommended an evisceration or enucleation. As a matter of fact since the patient refused an operation in the first of these cases, we were tempted to try this mode of treatment and the result was so satisfactory that we tried it on other similar cases. Briefly the results were

(1) The relief of pain was considerable, (2) The eye gradually became quiet though atrophied, (3) Although there was no hope of restoring any vision, the patients were spared an enucleation.

In the single case of Mooren's ulcer complicated by hypopyon, not only did the hypopyon disappear, but the ulcer ceased to progress. That should tempt us to try this therapy in an uncomplicated case of Mooren's ulcer.

The case of neuroparalytic keratitis with hypopyon was a total failure, and the probable cause was that the hypopyon was caused by Koch-Weeks' bacilli, as will be further explained presently along with the other failures.

Very lately indeed we have given thought to the treatment of trachomatous corneal ulcers with subconjunctival injections of soluseptasin, since the literature on sulfonamide therapy in trachoma is encouraging. Our case was one with secondary pyogenic infection, and the result was not discouraging. We will not add anything more to that until we have reported several summer-swallows instead of the solitary one we are reporting.

Commenting on our five failures we have the following explanations to offer—Firstly, local subconjunctival sulfonamide therapy is useful mainly for exogenic infections, and not so much for endogenic. Intelligent patients could always tell the level of anesthesia when

or an operation on the eye, the infection may be considered exogenic, and as such results can be expected. But those suppurations which result from a latent septic focus elsewhere and which get precipitated in the eye as a result of any form of trauma, sulfonamides orally and parentally by intravenous or intramuscular injections will act much better than local subconjunctival injections of the same.

In enophthalmitis, however, where the infection is probably endogenous, because there is no corneal wound or ulcer, subconjunctival soluseptasin therapy has proved unexpectedly satisfactory, because in every one of the four cases treated the relief of pain and disappearance of pus took place to a surprisingly good extent. However, vision could not be improved.

There is a form of iritis that gives rise to hypopyon, which really we should not have classified and reported under hypopyon ulcers as we have done, and in that case subconjunctival sulfonamide therapy proved worse than useless. The pain and the hypopyon both increased after its use, though later on both got less and ultimately disappeared with oral use of sulfathiazole.

Secondly, the patient himself must be able to put up a certain amount of resistance of his own. In the definition of hypopyon ulcer, we are accustomed to incorporate the statement that it takes place in weak elderly people of the working class, and in our series of cases most of them have been weak and immatulated, some more so than others, in fact one of them died. The destruction of the enemy with the help of foreign supplies and aid must be effective only in the presence of a will to fight, and a generous supply of arms from home-resources. Where local resources of offering resistance are poor you cannot stem the enemy's onrush by merely looking to foreign aid for supply and support.

Thirdly, sulfonamides have a selective action more on one set than on other sets of organisms. Examination of the conjunctival smear should be of great help in such cases. Only in one of our failures, the case of neuro-paralytic keratitis where organisms could only be found by a scraping of the ulcer itself they were found to be Koch-Week's bacilli—rather a rare organism to give rise to a hypopyon, and against which sulfonamides are impotent. So we can account for at least one of our failures, the offending organisms being probably sulfonamide-proof. Since in the other failures we were unable to detect organisms in the conjunctival smear we cannot say how many of those were caused by sulfonamide-resisting organisms. Examination of the scrapings of the ulcer itself, and a culture preparation from the same, would certainly have helped us more in that direction, as often we could not detect any organism only on a microscopic examination of the smear even in the presence of a large number of pus cells.

To compare the results of this form of treatment with those of the usual routine treatment, one of our cases afforded a unique opportunity. He developed a hypopyon ulcer in the left eye which was

treated on the routine lines, viz, carbollisation, milk injection, atropine, dionin etc. A bad perforation resulted with expulsion of lens and part of the vitreous. Then he developed a hypopyon ulcer in the right eye, and the eye was treated with subconjunctival soluseptasin injections, and it healed without perforation, within seven daily injections of the same.

The following may be considered the advantages of this new method over the old routine method —

- 1 That it is more certain in its action, at least about 75% responding favourably, but it acts better in the presence of certain pyogenic organisms than of the others
- 2 The effects are immediate, the very first injection relieves the pain, reduces the oedema and the hypopyon, in many cases
- 3 Organisation of the hypopyon into a fibrous mass cannot take place, because of the rapid disappearance of the hypopyon
- 4 Drastic measure like Soemisch's section, evisceration etc are not necessary
- 5 Perforations are less frequent and run a benign course if they do occur
- 6 Resulting opacity is thinner and the vision at the end much better

It only remains to compare the subconjunctival method of administration of soluseptasin, with the oral and parenteral methods

- 1 This method is economical, as no more than 2 grs of the drug are needed per day
- 2 With such a small dose there is no question of susceptibility to the drug and toxicity
- 3 The effect is where it is needed most i.e. local and also it is immediate
- 4 Since soluseptasin does not act readily in the presence of albuminous matter, local applications of soluseptasin in ointment or any other form are ineffective

#### CONCLUSION

By way of conclusion, I shall sum up that —

- (a) This method is very easy, effective, safe and comparatively cheap method of meeting a serious ocular condition for which hitherto the treatment has been far from satisfactory
- (b) Many eyes can be saved from total loss, and the end result after this form of treatment is much better than after the older methods of dealing with the same
- (c) In cases where there is no hope of restoring vision, at least the patient can be spared an enucleation or evisceration and above all it goes a long way for the relief of pain and misery

In his reply Dr. Cooper added that he felt that the action of soluseptasin given subconjunctivally was not only bactericidal but antiphlogistic and resolvent, which combined effect was the cause of the superiority of this method over the oral administration and parenteral injections of the same drug

# Case Reports

## AN UNUSUAL TYPE OF ENTEROLITH

by

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AND

B N PURADARE

M.D., F.R.C.S

The presence of bile stones in the intestine with or without obstruction is not a new finding both for surgeons and clinicians. References are therefore found in the literature often describing solitary cases when such stones have been encountered in the intestine at the time of the radiological examination or at the time of an operation. Sweet (1938) McQueeney (1939) and Greene and Hotz (1939) have reviewed the literature in this connection and have tried to explain the etiological factors leading to the stone formation. Phenister and Alonson (1941) have reported on chemical analysis of gall stones and have shown that the analysis differs in different individual and in the same individual at different times, depending upon the variation in the composition of the bile, the freedom of the flow, the site of stone formation and the pathological state of the gall bladder wall during the period of stone formation. But according to them, in almost all cases such stones are usually rich in cholesterol and contain only small amount of bile pigments, calcium, phosphorus and iron.

Although the formation of gall-stones and their detection in the gall bladder is a common finding the frequency of intestinal obstruction is rather low. McQueeney (loc cit) has shown that out of 7232 cases recorded the intestinal obstruction was found only in 149 cases, i.e. only in about 2 per cent of the cases. However in such cases mortality was as high as 50 per cent owing to delay. This delay is often caused because the preliminary signs are not alarming. There are occasional attacks of colic, epigastric pain, nausea and vomiting. Those may not repeat themselves for years until a sudden severe attack brings the patient to a doctor and then it is often found that the stone has grown to a considerable size and has caused intestinal obstruction. Dulin and Peterson (1939) have reported ten such cases some of which were fatal after the operation. The size of the stones described by these authors varied from  $2 \times 2 \times 2$  cms to  $7 \times 5 \times 5$  cms and in all cases there was a history of intestinal obstruction. The case reported here is interesting from the point of view of the size of the

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This work was carried out under the guidance of Dr V R Khanolkar, Director of Laboratories, Tata Memorial Hospital, Bombay

stone, the duration of its growth and its chemical composition. It presented the following clinical history

A married Hindu woman, 29 years old had been suffering from attacks of pain in the abdomen from the age of twelve years but the pain had ceased for the last three years. The pain was mostly in the evening and lasted for 3 to 4 hours in the region of the umbilicus, wandering in somewhat clockwise circular movement and accompanied by gurgling sound and occasional vomiting. History of amenorrhoea of 11 months. The patient consulted a doctor in 1928 and was advised to get the mass felt in the right iliac fossa removed. It was suspected to be tuberculosis of the ileo-cecal junction. The patient was unwilling for an operation. The uterus at that time was found small and retroverted. Since that time till the removal of the stone in December, 1942, the patient was being prescribed various sorts of medicines such as cod liver oil, liver extract pills, calcium gluconate, insulin by injections and various patent tonics such as palol, aswan, sanatogen and ashoka cordial. A lump was felt by the patient since September, 1942, and because of the presence of amenorrhoea suspected herself to be pregnant. In December 1942 the patient was referred to one of us (B.N.P.) for amenorrhoea and suspected pregnancy. P. V. examination showed a hard mass of the size of a cricket-ball in front of the uterus which was in the pelvis. It was freely moveable, and the uterus was not enlarged. Plain x-ray of the abdomen showed a calcified tumor occupying the pelvis. Diagnosis was given as no pregnancy, but tumor in the pelvis probably dermoid of the ovary or pedunculated calcified fibroid of the uterus. An exploratory laparotomy was advised and the operation was performed on 31-12-42.

*Findings at the Operation* —On opening the abdomen by sub-umbilical midline incision under spinal anaesthesia, a mass of the size of the cricket-ball was seen to occupy the pelvis. On delivering it out of the abdominal incision it was found to have no connection with the genital organs, which were found to be practically normal but for retroverted condition and small size of the uterus. The mass was situated about two feet proximal to the ileocecal junction and there was no alteration in the appearance of the intestine either proximal or distal to it. The mass was found to be moving freely in the lumen of the intestine and hence the intestine was incised and the stone removed. The patient made an uneventful recovery.

*X-ray Examination* —A plain x-ray of the abdomen, taken few months after operation did not show presence of any stone. Cholecystography showed normal gall-bladder without any gall stone.

*Description of the Stone* —The stone was dirty yellow in colour, hard to feel and was almost of the size of a cricket-ball. It was about two feet above the ileo-cecal junction, freely movable within the lumen of the intestine. The x-ray of the stone showed a deeper shadow of the size and shape of the two anna piece in the centre with faint concentric rings surrounding it. Fig 1 and 2 show the photographs of the stone and its x-ray picture. The stone had an

average diameter of 8.5 cms. The surface was coarse but granular and at places it was shining probably on account of some crystalline ingredient. When it was cut into two equal parts the cut surface presented the appearance of typical concentric rings (Fig 3), known as Liesegang's rings. These rings divided the centre cross section into four zones differing from one another in hardness and the depth of colour. In the centre was a square shaped black material which was opaque to x-ray (Fig 2). On casual examination this square-shaped material gave an impression of a remnant of the outer shell of a tamarind seed. In order to throw some more light on the nature of the stone a careful chemical analysis was carried out.

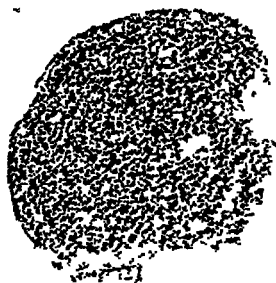


Fig 1

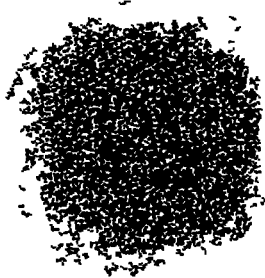
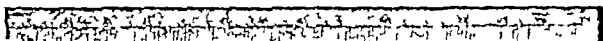


Fig 2



3

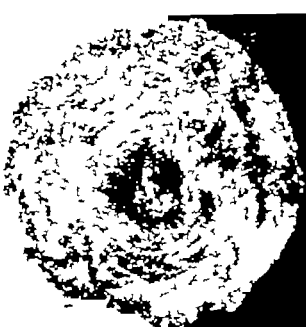


Fig 3

**Chemical Analysis of the Stone** —The total weight of the stone was 185.5 gms. The four zones mentioned above were mechanically separated and chemically examined. The general scheme of analysis was that recommended by Hawk and Bergeim (1938) with so



modifications      The results of analysis are given in the following table

Constituent %	First Layer	Second Layer	Third Layer	Central Layer
Moisture	8 50	8 20	5 00	3 80
Cholesterol	16 35	18 35	19 00	18 80
Pigments	1 65	1 67	2 59	3 35
Glycocholic Acid	73 19	71 73	73 30	74 00
Inorganic Material Ca, P and etc.,	Traces	Traces	Traces	Traces

## DISCUSSION

The present case was interesting for two reasons. Firstly the stone was of a long duration and was detected in the intestine without any clinical signs suggestive of an obstruction or any appearances at the operation showing its escape from the gall bladder into the intestine through a biliary fistula. Secondly the composition of the stone did not fit in with that of the stones usually found in the gall bladder (high cholesterol content). If these two factors are taken into consideration, one is inclined to think that the process of formation of the stone was probably different from that of a typical gall stone. Provisionally it may be said that the tamarind seed formed a nucleus round which the bile got deposited and finally formed a stone. This assumption is liable to two objections (1) It has not been possible to establish the exact nature of the portion which resembles in gross appearance the tamarind seed. The histological preparations do not yield a definite structure owing to the long stay in the intestinal lumen and the action of the intestinal juices on it. The sections were shown to Prof Shevde and he is of the opinion that the appearance is suggestive of the structure of the outer layers of the seed. The chemical studies also suggest—in a negative way—that the material is derived from a vegetable seed and is not formed from the deposition of crystalline surfaces round albuminoid material. (2) The factors which prevented the passage of the seed down the intestine when the stone was still small in size. No satisfactory explanation could be given for this except for the fact that the patient was suspected of the tuberculosis of the ileocolic junction which might have probably reduced its normal dilating capacity and hindered the tamarind seed or the stone from passing out. If this explanation is accepted it is also easy to visualise the stone formation. Under such circumstances the flow of the bile with the digested food material was slower than in the normal individuals and this has probably further facilitated the deposition of the bile on the seed.

The second point of interest is the chemical composition of the stone. Majority of gall stones described in the literature are rich in cholesterol. The present stone contained a large proportion of glycocholic acid. It is true that the normal human bile is rich in glycocholic acid and contains lesser amounts of taurocholic acid. The

glycocholic acid is more insoluble of the two but in the bile these acids are present as their sodium salts and as such the stone should also contain some taurocholic acid. The high proportion of glycocholic acid in the stone could however be explained by the fact that no sooner the bile finds its way into the intestine its various components get diluted and probably the sodium salts get ionised setting free the true acids and then the insoluble acid got deposited in the stone under suitable conditions. An alternative explanation would be that the composition of the bile secreted by the patient was probably abnormal. It contained more glycocholic acid which got deposited preferentially, when a suitable nucleus was available. But in the absence of any other metabolic disturbances in the patient it appears that the former explanation is more likely.

**Conclusion**—A case of stone in small intestine of a large size, peculiar chemical composition and presenting unusual clinical features without obstruction, has been described. Probable etiological factors leading to formation of such stones are discussed.

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# *Society Proceedings*

The 35th Scientific Meeting of the G S Medical College Staff Society, Bombay, was held on the 11th March, 1944 at 9 p.m (ST) in the Main Lecture Theatre of the College Dr N D Patel was in the chair Dr K. A J Lalkaka gave

## **A DEMONSTRATION OF HYPNOTIC AND POST-HYPNOTIC PHENOMENA**

My object in demonstrating these phenomena to-night is to emphasize two significant psychological facts—

1 The important role of suggestion—conscious and unconscious—in the production of various symptoms and states relating to the voluntary and involuntary systems of our body, and

2 The existence of the unconscious mind as revealed during the carrying out of post-hypnotic suggestions, where the subject is unconscious of the real reasons that prompt him to do a particular action

Suggestion, in popular language is described as a seed which when planted in a favourable mental soil, takes root and grows into a tree Psychologically, suggestibility is described as the capacity to accept an idea without adequate logical reasons In hypnosis there is a markedly enhanced state of suggestibility, and the same thing often occurs in acute illnesses, as well as in states of mental and physical stress

I may be pardoned for quoting a few relevant examples

1 Case of Mrs M D M where an acute attack of diarrhoea developed soon after hearing the news of her friend getting a similar attack

2 Case of Mr J D He had for some time developed pill-rolling movements of the right thumb and index finger He got bed-ridden and died a few weeks after listening to the talk that took place between two of his physicians during a consultation over the differential diagnosis of his complaint No amount of persuasion later on, on the part of the physician, could alter his conviction that he was suffering from all the diseases that were discussed during the consultation

The moral is that diagnosis and prognosis should not be discussed in the presence of the patient

In treating a case with hypnotic suggestions, it is very necessary to overhaul him physically first, then do a psychological analysis to find out all the conscious and unconscious factors responsible for the symptoms Otherwise, the symptoms are very likely to recur as the patient is not made aware of the causative factors

In some cases, particularly of recent psychological traumata, as for example, cases of war neurosis, the psychological analysis could

with advantage be done in hypnosis, before hypnotic suggestions are given. During analysis, abreaction takes place, i.e., while re-living the past painful experiences, a discharge of repressed emotions occurs, and with it there comes a certain amount of relief of symptoms.

Persons who are unco-operative, suspicious, inattentive or who are suffering from psychosis or mental deficiency are difficult and unsuitable cases for hypnotism. Willing, intelligent persons with good concentration make much better subjects.

Hypnotism is an artificially enhanced state of suggestibility resembling sleep, wherein there appears to be a normal dissociation of the conscious from the sub-conscious elements of the psyche (mind), conditioned by and dependent upon a state of voluntary co-operation and harmony between the subject and the hypnotist.

Hypnotism is largely a condition of great concentration and more or less profound abstraction. There occurs an unusually great or extraordinary concentration of attention on the subject or train of thought, which may be extremely limited, or vague and extensive, with complete unconsciousness or disregard of the rest of the external world.

Though hypnotism has been known of for many centuries, its nature was not properly understood and it was attributed to magic.

In hypnosis, a person becomes capable of influencing all his bodily functions, increasing or delaying their activity, producing anaesthesia or hyperaesthesia as desired.

Charcot believed that psychoneurotics alone can be hypnotised. Bernheim demonstrated that normal persons can also be hypnotised. In order to bring about hypnosis and influence a subject therapeutically, the most important thing is to produce the right emotional atmosphere. The more feeling we can throw into our words, actions and manner, the greater will be the influence.

As regards stages of hypnosis, the following classification of Forel seems most convenient:

1 Somnolence—Resistance is only possible with an effort and there is no loss of memory.

2 Light sleep or hypnosis—The eyes are fast closed and resistance is impossible, but there is still no loss of memory.

3 Deep sleep—Somnambulism—In this stage post-hypnotic phenomena are obtained more readily than in the second stage. There is amnesia.

In hypnosis the subject is in a state resembling sleep but this is quite different from natural sleep. In hypnosis the subject remains in touch with the operator whose voice he constantly hears and whose suggestions he carries out. If the subject goes into the third stage he has no recollection of what he did or what was said to him. All the same he remembers to have heard constantly the deep and soothing voice of the hypnotist.

#### *Case Reports*

*Case I* The subject was hypnotised and the following was brought out —

- 1 Paralysis was produced in his right leg and as a result of post-hypnotic suggestion, it persisted after coming out of the trance, disabling him from walking
- 2 Inability to open his fist or move his joints when such a disability was suggested
- 3 The autonomic nervous system was influenced, leading to acceleration of the pulse by 20 beats per minute while the patient was lying quietly recumbent This was done by suggesting to the subject that he was chasing a rabbit
- 4 Anaesthesia which enabled a pin to be passed through a fold of skin on the fore-arm
- 5 Carrying out of other post-hypnotic phenomena automatically, about the motive of which he had no conscious knowledge

*Case II* In addition to many of the phenomena produced in the first subject, the following were elicited

The subject was taken into the somnambulistic stage where, though apparently awake and on his feet, he was really in a trance and accepted various suggestions

- 1 Reproducing the toxic effects of alcohol like tumbling, swaying and vomiting as a result of administering water with the suggestion that it was alcohol
- 2 Change in gustatory emotion, sugar tasting extremely bitter when it was suggested to be quinine
- 3 The subject was made to deliver an oration on the ill effects of alcohol before an imaginary audience
- 4 Post-hypnotic suggestions were also carried out

#### THERAPEUTIC USES OF HYPNOTISM

- |  |   |
|--|---|
| 1 Hypno-analysis for   | 5 Spasmodic affections like Asthma  |
| (a) War Neuroses (Shell Shock)   | 6 Neuralgias  |
| (b) Other forms of traumatic neuroses  | 7 Headaches   |
| Here recovery of the painful, forgotten memories and the reliving of the associated emotions (abreaction) occurs       | 8 Insomnia  |
| (c) Amnesia (Recovering of forgotten memories)   | 9 Stammering (Functional)   |
| 2 Somnambulism or sleep-walking  | 10 Psychotherapy—For giving encouraging suggestions of a general and specific type under hypnotically relaxed mental and physical state |
| 3 Fugues and Dual Personalities  | 11 Anaesthesia—for surgical purposes.   |
| 4 Various Hysterical conditions—'Conversion Hysteria' Deafness Aphonia Anaesthesia Paralysis Vomiting Convulsions, etc | 12 For producing a condition akin to twilight sleep   |

#### DISCUSSION

**Prof R G Dhayagude** asked whether the subjects were conscious of what was happening to them

**Dr Lalkaka** said, that in the first and second stage they are conscious to a varying extent but not in the third stage

**Dr G M. Phadke** mentioned a case where a hernia operation was done under hypnosis

**Dr S G Joshi** wanted to know whether hypnotism could help cases of stammering The answer was that it was possible in cases of the functional type Early cases were more suitable for treatment

Dr H S Mehta wanted to know whether under hypnotic influence criminal acts could be suggested. Dr Lalkaka replied that in hypnotism as practised under mutual co-operation, the subject resents doing actions that offend his moral code. He quoted an example of a young female when asked to undress before a class of students came out of the trance in a rage, though unconscious of the reason for her anger. Dr H S Mehta also asked whether if a criminal was hypnotised, the material given out by him would be considered adequate evidence for conviction. In reply the speaker said that it was extremely difficult to hypnotise a person against his will and it was doubtful if the material brought out under such conditions could be relied on.

Concluding the discussion, Dr N D Patel complimented Dr Lalkaka on his very instructive demonstration and remarked on the part played by suggestion, conscious or unconscious, in the causation of symptoms. The importance of recognising this fact could not be over-emphasized in clinical work. Anxiety neurosis with its multiplicity of symptoms, psychalgias of varying intensity, vomiting, dysmenorrhoea, cancer-syphilis-disease-phobias with typical syndromes were of daily occurrence in clinical practice. Forty years ago, the medical student was made to enter the temple of medicine through the portals of bacteriology, and the text books of medicine began with description of infection and infectious diseases (vide Osler's and Price's *Practice of Medicine*). To-day the changed attitude of the medical thinkers is reflected in the last edition of Osler's classic, revised by Christian, which begins with a discussion of the role of mind in the production of symptoms. The medical student is made to study normal and abnormal psychology before he enters the wards. In fact, now he is made to enter the medical world through the portals of psychology, and I am sure, he can hope for no better guide than Dr Lalkaka in his voyage of exploration.

# Report of the Clinical Conferences

AT THE TATA MEMORIAL HOSPITAL, BOMBAY

Conf on 3-3-44

A case († 6372) of **Localised Osteitis Fibrosa** presented by **Dr J C Paymaster**. A 35 years old chinese male with a definite history of repeated trauma to the right knee. The first trauma occurred in January 1942. Recently he had developed some sort of pain in the upper end of the right tibia. There was no history of fever at any time. Examination revealed a swelling of the upper end of the right tibia the right knee joint was absolutely free. The swelling felt warm to touch, and slight tenderness could be elicited. The clinical diagnosis was either a "Benign giant cell tumor" or an "osteogenic sarcoma" but since the x-ray pictures revealed cystic enlargement of the upper end of the tibia, the diagnosis was more in favour of a benign giant cell tumor. A formal biopsy was performed. At the time of biopsy, a soft, yellow coloured material was obtained which was quite different from the type that one usually got in benign giant cell tumors. Microscopic examination, together with the clinical and radiological findings now suggested it to be "localised osteitis fibrosa". Blood chemistry revealed alkaline phosphatase raised to 42 Bodansky units, the rest of the findings were normal. Amongst the clinical differential diagnosis, an "atypical type of tuberculosis" was mentioned. The most suitable line of treatment which was suggested consisted of scooping out of the cystic areas and filling them with bone grafts. Dr Paymaster, referring to literature said that the recurrence rate with such a method of treatment was given by some well known authors as high as 32%.

A case († 6180) of **Tuberculosis of Sternum** presented by **Dr D R Meher-Homji**. An 11 years old boy who came to the hospital on 29-1-44 with a history of swelling of the sternum of twenty days' duration. On examination, it was found that there was a swelling involving the manubrium sterni, which was smooth on surface, firm in consistency and slightly tender on pressure. A clinical diagnosis of Ewing's tumor was made and the patient was admitted to the hospital. Blood studies revealed no abnormality, calcium, phosphorus and phosphatase were within normal limits. Kahn test was negative. X-ray picture of the sternum revealed rarefaction with periosteal proliferation at right angles, suggesting bone tumor. An aspiration biopsy was done and was reported by Dr Khanolkar as chronic inflammatory osteoperiostitis. He was placed on potassium iodide mixture for fifteen days, but showed no diminution in the size of the tumor. At the time of presentation of the case to the conference, there was a definite fluctuation in the upper part of the swelling. The general opinion was that it should be considered as a case of tuberculosis of manubrium sterni and Dr A V Balga agreed to take over the case at the King Edward Memorial Hospital. The patient was operated by him on 14-3-44 for excision of manubrium sterni. The material sent for histological examination showed the following characters

**Gross Examination** "Several pieces of tissue firm to feel and greyish in appearance. Hard bony spicules accompany the material. **Microscopical Examination** showed diffuse exudate of plasma cells, lymphocytes and histiocytes. There were a few discrete foci of productive granulation tissue with proliferated epithelioid cells. Multinucleated giant cells were seen in these areas with areas of caseation. Tubercle bacilli could not be demonstrated in sections stained by Ziehl-Neelsen stain. The tumor cystology was suggestive of *Tubercular Osteomyelitis*."

A case († 6383) of **Malignant Tumor of the Frontal Sinus** demonstrated by **Dr E J Borges**. A woman of 53 years developed a swelling at the root of the nose on the right side, two months ago which rapidly increased in size. It invaded the orbit, obscuring the eyeball and filling the temporal region. A month ago she developed bilateral pre-auricular nodes. An aspiration biopsy of the tumor showed malignant cells. The nature of this tumor was discussed and the probable diagnosis of carcinoma of the frontal sinus was made. The remarkable absence of any nasal blockage or discharge was pointed out. Reference to literature<sup>1</sup> showed that only 37 cases of cancer of the frontal sinus had been recorded upto 1937. It was decided to take a formal biopsy of the lymph nodes for a histological diagnosis and in the meanwhile, to treat the patient palliatively with deep x-rays. The biopsy from the left pre-auricular node was reported as carcinoma of a low grade of differentiation, resembling the type described by Quick & Cutler<sup>2</sup> as "transitional cell carcinoma."

A case († 6430) of **Swelling over the region of the right shoulder** presented by **Dr D J Jussawalla**. A 32 years old man complained of a swelling over the right shoulder for one year without any history of trauma. The swelling did not give him pain so that it was neglected for about six months. On physical examination soft, elastic, pseudo-fluctuant masses were felt in the right supraclavicular and suprascapular areas. There was venous engorgement of the right upper extremity. No abnormal signs were detected in the nervous system. The case was presented for clinical diagnosis. **Dr A V Baliga** suggested it to be a fibrosarcoma. **Dr Khanolkar** was of opinion that it was a neurogenic sarcoma. **Dr Jussawalla** commented on the case and said that in view of the long history, absence of signs referable to the nervous system and the physical characteristics, the tumor would most probably be a liposarcoma. A biopsy was taken on 4-3-44 which was reported as follows—The *microscopical examination* shows that the tumor tissue is made up of cells with indefinite cytoplasmic outlines enclosing round or ovoid nuclei. The nuclei contain uniformly scattered chromatin material. There is only a moderate degree of variation in the size of nuclei. Frozen sections stained for the presence of lipid material do not show the presence

<sup>1</sup> Breeding E G. Malignancy of the nasal accessory sinuses with a report of two cases of primary carcinoma of the frontal sinuses. *Ann Otol Rhin and Laryng*, 49, 141, 1940.

<sup>2</sup> Quick & Cutler, Transitional cell epidermoid Ca, *Surg Gynec & Obst*, 45, 320, 1927.



of Scharlach R stained material in the cell cytoplasm. There is no new formation of reticulum. The tumor cytology is suggestive of *Neurogenic Sarcoma*.

Dr. R Naidu initiated a discussion on a study of the carcinoma of cervix. Dr. J C Paymaster dealt with the clinical aspects of the disease and stated that among the first 5000 cases seen in this hospital 300 cases were found to have carcinoma of the cervix. But out of this total of 5000 the number of patients suffering from malignant disease was only about 3000. Therefore the incidence of the carcinoma of cervix to the total number of malignant cases was close to 10%. Two hundred patients out of these 300 received treatment at the hospital. About 50 received roentgen therapy alone and since such treatment could not control the disease, these cases were not included in the discussion. Out of the remaining 150 patients 36 received irradiation through radium alone while the remaining 114 received combined radium and roentgen therapy. He pointed out the main presenting symptoms in these patients as follows:

1	Vaginal bleeding alone	21 cases
2	Vaginal discharge alone	33 "
3	Vaginal bleeding or discharge together with pain in back, lower abdomen or thighs	48 "
4	Vaginal bleeding or discharge associated with pain in addition to difficulty or change in bladder or rectal function	44 "
5	Pain alone	4 "

All the cases were grouped according to the clinical classification formulated by the League of Nations which takes into consideration the four stages as shown in the following table:

Stage I:	The carcinoma is limited to the cervix. The uterus is movable and no para-cervical induration is detectable. It may be big or small, may be an ulcer or cauliflower growth.
Stage II:	The carcinoma has extended to the vagina, parametrium and corpus.
Stage III:	The disease has <ul style="list-style-type: none"> <li>(a) Extension to the parametrium and pelvic wall</li> <li>(b) Extension to lower 1/3rd of vagina</li> <li>(c) Isolated pelvic metastases</li> </ul>
Stage IV:	The disease includes: <ul style="list-style-type: none"> <li>(a) Involvement of bladder</li> <li>(b) Involvement of rectum.</li> <li>(c) Distant spread.</li> </ul>

It involves most of the vagina and has metastasised beyond control.

The distribution of our cases according to the classification was as follows:

League of Nations Classification Stage	Number of patients	Percentage.
I	35	11.7
II	77	25.6
III	106	35.3
IV	82	27.4
All Stages	300	100

Dr. R Naidu described in detail the protocol of treatment by radiation. When the pathological investigations corroborate the clinical findings then only does the treatment commence. Irrespective of the stage of the disease the patients are treated first with radium whenever possible because radium alone can destroy the primary cancer. But in actual practice in a great majority of cases X-radiation has to be administered first owing to the extensive and in-

fectured nature of the lesions which make the application of radium extremely difficult

Radium is administered through one of the many types of vaginal bombs directly in contact with the cervix and the dose delivered is 1,500 mc-hours of Gamma-radiation, filtered through 0.5 mm of platinum and 1 mm of brass. This is followed the next day by the insertion of a cervical tandem containing 2 radon capsules in the uterine canal and a further dose of 3000 mc-hrs is given. The vaginal bomb is so designed that the beam of gamma-rays can be easily orientated so as to irradiate the primary lesion whatever its anatomical position. The healthy tissues in the neighbourhood are substantially protected from radium rays by about 1 cm of lead screen built into the bomb. The strength of the radon capsules with their platinum jackets, in the cervix tandem is such that the lower source is twice as strong as the top one.

The amount of radiation administered through these two applicators is sufficient to completely destroy all malignancy within a radius of 3 cm from the centre of the cervix. However tissues beyond this distance are also irradiated but the dose is not cancericidal and hence the necessity for supplementing it by X-radiation to the parametrium and to other parts of the pelvis. Whichever treatment is given first there is always an interval of 3 to 4 weeks in between so as to enable the peak reaction to subside.

While discussing the cycle of x-ray treatment of Ca cervix, Dr Naidu stated that the routine settings in this hospital were 200 KV constant-potential, 15 milliamperes of tube current, 0.5 mm Cu plus 1 m Al filter, and 50 cm Target-skin distance. The radiation output under these conditions was 70 roentgens per minute as measured in air at the skin level. Radiation was administered according to the divided dose technique using 4 or 6 fields of 10 x 15 cm each. 200 to 300 roentgens were delivered per portal and one to two fields were treated daily. The full dose being 2000 to 2500 roentgens per field the treatment cycle takes 7 to 10 weeks for completion. This long interval of time implied in this technique made it desirable that radium be applied first whenever possible so as to sterilize the primary lesion at the beginning of treatment.

The choice of the number of fields depended on the nature of the disease and the condition of the patient. Treatment with four fields (2 anterior and 2 posterior, with 2 cm gap between the fields on the same side) was given to thin patients and to those with advanced disease where only palliation was possible. Treatment with six portals (four as above and two lateral) was given to corpulent women and to all favourable cases.

Discussing the merits and demerits of different techniques such as the massive dose, the divided dose and the pyramidal dose techniques Dr Naidu pointed out the need for varying the mode of treatment to suit individual patients and suggested an increase of the Target-skin distance from 50 to 70 cm so as to double the depth dose.

in the whole pelvic region This method of increasing the depth dose was contrasted with that obtained by increasing the filtration from 0.5 mm to 2.0 mm of copper

Dr R. T Subramaniam described the results of treatment by radiation in 150 cases of carcinoma cervix These results could not be compared with published data from similar institutions in other countries as the total period of observation here had not exceeded 3 years The results are summarised in the two following tables It should be noted that patients who received 75% or more of the prescribed dose of radiation are included in the category of those who had received full treatment The average dose of radium administered to this group was 3622 millicuries

L O N classification stage	No of pts. who received full treatment.	No of pts with no evidence of disease at their last examination.	No of pts with very good regression.	No of pts with disease at last examination.	No of pts. who are followed at present.	No of pts who were not followed
I	21	12	3	1	5	
II	37	15		18		4
III	22	6		12		4
Total	80	33	3	31	5	8

Patients in whom the disease had extended to stage IV L O N were not included in the review as there was no attempt at a curative treatment in those cases and any radiation which was administered was purely by way of palliation mainly for the relief of pain, infection or bleeding The total period of observation in patients without any evidence of disease after treatment is shown in the following table

L O N Classification	No of pts who have no evidence of disease.	PERIOD			
		Below 6 months	6 to 12 months.	12 to 18 months	18 to 24 months.
I	12	6	3	2	2
II	15	11	2	2	
III	6	5			1
Total	33	22	4	4	3

The results were compared with the 5 year survival rates of other well known clinics The patients who did not attend the follow up clinics are not included

Stage L O N	T M H Bombay	Memorial Hospital New York.	Marie Curie Hospital London	L O N Report 1938
I	75%	78.2%	86.1%	55.2%
II	40.5%	42.8%	62.0%	30.8%
III	33.3%	26.5%	32.1%	21.2%
IV			8.5%	5.8%

Dr V R Khanolkar dealt with the histology of the 300 cases of cancer cervix which had been studied in the pathology department The histological grouping was based on the types suggested by Martzloff<sup>3</sup> and is tabulated below

	Prickle cell	Transitional cell	Spindle cell	Adenocarcinoma	Total
Kelly Clinic	6	77	13	4	704
T. M. H.	10	72	16	2	300

The distribution was compared with that published recently from Kelly Clinic in Baltimore by Jones<sup>4</sup> Dr Khanolkar mentioned that at a recent meeting of the Bombay Obstetric and Gynecological Society<sup>5</sup> an opinion had been expressed that the treatment of cancer of cervix depended upon the clinical stage of the disease and not on the pathological grading. He said that this was evidently an erroneous opinion as the treatment depended both upon the anatomical extension of the disease and the histological characters of the tumor. He showed a table showing the cure rate in patients from Martzloff's series who had a Wertheim operation performed on them and from Jones' series who had been treated by radiation alone. All the cases were clinical stage I and it could be seen that adenocarcinomas were best treated by surgical methods, the transitional cell types gave incomparably better results with radiation. A difference of opinion could only exist in the prickle cell type as to whether the treatment should be by surgery or by radiation.

CURE RATE IN RELATION TO HISTOLOGY

			Prickle cell	Transitional cell	Spindle cell	Adeno- carcinoma	Total
Martzloff (Wertheim Operation)	Cases	treated	50	259	47	28	379
	Cases	cured	23	63	5	17	108
	%	cure	47	24.2	9.2	75	28.5
Jones H W et al (radiation)	Cases	treated	6	64	11	6	87
	Cases	cured	2	37	10	1	50
	%	cure	33	58	91	16	57.5

Dr B N Purandare in the course of discussion which followed said that carcinoma of cervix should not be considered as a single entity but should be clinically grouped into 16 types according to the four clinical stages and four histological sub-groups. He agreed with the opinion expressed by Dr Khanolkar regarding the treatment of adenocarcinoma, transitional cell and spinous cell types. He was however, of opinion that the incidence of spinous type of growth was greater in Indian patients and that L.O.N. stage I and II cases of spinous cell as well as the adeno-carcinoma would be best treated by operation. The stage I cases of the other two types should be treated by radiation with operation. The operative mortality in his hands as well as of other surgeons in stage I cases had been negligible. With vaginal hysterectomy (Schauta's operation) the operative mortality was still lower and deserved consideration in the line of treatment.

Dr E J Borges, in reply to Dr Purandare, stated that the adenocarcinoma and prickle cell types which Dr Purandare wished to see treated surgically, constituted only 12% of the whole group, and of these 12% a very small percentage came in the clinical stage I and II in which alone surgery could be considered. In actual practice therefore, the number of cases in which a radical operation was indicated was very negligible. Thus radiation still remained the treatment of choice.

4 Jones Howard W., and Seegar Jones, J.A.M.A., 122: 931, 1943  
5 Pool, J L., Medical Bulletin, 11: 403-409, 1943

# Proceedings of the Radiological Section

2nd BOMBAY MEDICAL CONGRESS, AT C J HALL ON FEB 21, 1944

## X-RAY DIAGNOSIS OF BONE TUMORS

A resume by L H ATHLE, M B B S, D M R, M A C R

(From the Department of Radiology, Tata Memorial Hospital Bombay)

X-ray examination is a very important method in the diagnosis of tumors of bone, especially so when histological examination is not possible for any reason. The most important issue to be decided is whether a tumor is malignant or not. There are no definite criteria which can by themselves decide the point. Changes like destruction of bone, new bone formation, periosteal reactions, right-angled bone formation, onion-peel appearance, can be seen occasionally in non-malignant conditions as well. There are certain minor differences in the nature of these changes which may suggest the real nature of the lesion. For example the right-angled bone formed in osteogenic sarcoma tends to consist of fine striations parallel to each other. In chronic osteomyelitis these are irregular, blunt and of unequal length. In syphilis, periosteal bone forms wavy outlines and looks like lace work.

Several radiograms of different types of osteogenic sarcoma were shown and compared with chronic osteomyelitis, syphilitic osteoperiosteitis and Garre's sclerosing osteomyelitis.

Ewing's tumor is not uncommon as shown by its incidence in the Tata Memorial Hospital series. There were 9 cases out of a total of 36 proved primary malignant tumors of bone. The appearances described as "typical" of Ewing's tumor are uncommon. Clinically as well as radiologically this lesion can simulate osteomyelitis. This fact is well known and duly recorded in surgical and radiological literature. It is not realised that soft tissue sarcoma and osteogenic sarcoma may be closely mimicked. In the Hospital series given below only one case showed the typical lesion, three were like soft tissue sarcoma secondarily invading bone and two were like osteogenic sarcoma. Radiograms of these lesions were demonstrated.

The differential diagnosis, of malignant giant cell tumors, solitary metastatic lesions producing a picture of a primary tumor and of other unusual lesions, like solitary myeloma was then discussed. At the Tata Memorial Hospital 72 cases of suspected primary bone tumors were seen. These were finally classified as under —

Osteogenic sarcoma	13	Malignant giant cell tumor	1	Chondroma	2
Chondro sarcoma	4	Metastatic tumor	3	Fibroma	1
Fibro sarcoma	1	Multiple myeloma	4	Adamantinoma	2
Ewing's tumor	9	Soft tissue sarcoma	5	Dental cyst	2
Reticulum cell sarcoma	1	Benign giant cell tumor	7	Eosinophilic granuloma	
Angio-endothelioma	1	Osteoma	2	of bone	1
				Chronic osteo-myelitis	11

Eleven cases of chronic osteomyelitis were referred clinically diagnosed or suspected as bone tumors. These were all diagnosed

correctly on x-ray examination. Most of these had regular biopsies confirming the radiological opinion.

*Conclusion* —(1) Detailed study and co-relation of all the x-ray appearance is necessary for greater accuracy in diagnosis

(2) There are no rigid criteria of malignancy

(3) Ewing's tumor is not uncommon in this country. It is missed many times because of the non-recognition of its protean manifestations

## RADIUM IN NON-MALIGNANT CONDITIONS

by M. D. JOSHI, D.M.B.E.

### UTERINE HAEMORRHAGE

Intrauterine treatment with radium gives excellent results in conditions where excessive uterine bleeding without any demonstrable gross pathology, is present, such conditions are menopausal, essential myopathic or idiopathic haemorrhages. Uterine haemorrhages due to malignant conditions or adnexal disease or inflammation or due to general systematic disorders are not included in this group.

Menopausal haemorrhage associated with large boggy uterus can be treated most satisfactorily with radium. It is almost a specific. The dose is 1200 mghrs and should rarely be exceeded. In young women desirous of having children the dose of 500 to 700 mghrs should be given to avoid premature climacteric or complications of labour should a pregnancy follow. The dosage of uterine haemorrhage in young girls is about 300 mghrs.

Tubal sepsis and sub-mucous polypi are contraindications for radium therapy.

In few cases there is sometimes bleeding within a fortnight after radium treatment, such cases should be treated medically. The bleeding stops within 2 or 3 days. If after 3 months the bleeding does not stop completely, another radium exposure may be required. But such cases are extremely rare. The technique of radium treatment is as follows. 50 mgs of radium with a filter of 0.6 mm platinum is put in a thin rubber tubing about 2 inches long. Extra half an inch of rubber tubing is kept without radium. This part comes in contact with the cervical canal when radium is introduced into the uterine cavity and prevents the possibility of stenosis of cervix and upper part of vagina. In introducing the radium into the uterine cavity the cervix is dilated and uterine cavity curetted and hot intra-uterine douche is given to control haemorrhage and remove debris. Curetting helps also in establishing the diagnosis whether the condition is malignant or non-malignant. Radium applicator is then introduced into the uterine cavity and vagina is packed with one long piece of gauze. Urine should be removed with a catheter every six hours and patient should lie in bed till the radium is removed.

In some cases there is sensation of vomiting due to foreign body in uterus which can be checked by administration of soda bicarb. In radiological literature there is not a single case on record where a woman after radium treatment has given birth to a deformed child.

It is said in the case of human beings there is all-or-none phenomenon in this respect. If a woman remains pregnant after she receives 1200 mghrs dose of radium the woman should be sent to hospital for delivery. The lower uterine segment does not dilate properly and surgical intervention may be required. With smaller doses there is no such difficulty and deliveries are normal and healthy normal babies are born. It is observed that cases treated with radium with 1200 mghrs dose sometimes begin to menstruate normally after 12 to 18 months. This proves that the ovarian function is not much affected. Deep x-rays are also used in treating uterine haemorrhages.

#### SPRING CATARRH

The disease the etiology of which is obscure, occurs chiefly in young children and more often in boys. It may affect palpebral or ocular conjunctiva or both. It is characterised by the presence of numerous hard flattened polygonal areas "pavement granulations" usually situate on the upper tarsal conjunctiva the lower lid not being so frequently attacked. The colour of the affected area is a bluish white the overlying epithelium being thickened. The course of the disease is very chronic and it tends to return in spring and autumn. Eosinophil leucocytes are generally present in large numbers and may often be found in the conjunctival secretion.

A needle containing 10 mgs of radium element with a filter of 0.6 mm platinum is placed in a rubber tubing. The lid is everted and the needle is held at  $\frac{1}{2}$  cms distance from the conjunctiva and kept moving on the everted lid. The sitting lasts for 5 minutes on each eyelid and it is given once a week. Six such sittings are generally required. Some cases require one or two more. The results are quite satisfactory. There is no inflammatory reaction of the conjunctiva due to radium exposure and the patient can attend to all his daily work without any inconvenience.

#### TUBERCULAR GLANDS

Treatment by Gamma rays of radium should be given superficially where the glands are enlarged. As these patients are generally weak and anaemic, small and frequent doses give good results. The treatment is contra-indicated if the patient is getting fever and if there is lung affection. Treatment should be continued till the glands have disappeared or until a small fibrous nodule results. Treatment is simple and without any danger. When suppuration occurs, the pus should be let out before it is treated with radium.

The dose for killing the Tb Bacillus is very big and being harmful to other tissues is not practical to apply. However, it has been noted that cultures of Tb Bacillus which has received a relatively short irradiation have their vitality inhibited and that sub-cultures made from these, grow much more slowly than controls. It is probable therefore that the radiation of Tb glands weakens the vitality of the Tb Bacillus and enables their destruction to be more readily accomplished by the phagocytic cells. Further the radium radiation acts as stimulus to the production of fibroblasts with the consequent

formation of an encircling and constricting fibrosis

Side by side with the radium treatment, efforts must be made to raise the resistance of the patient by attention to his general health

X-rays are also used for treating T.B glands, but in children it is very difficult to keep them steady while x-ray exposure is being given. In such cases radium is of great use

#### EXOPHTHALMIC GOITRE

Here also good results are obtained with radium treatment and it should be employed where for any reason operation is not feasible or is refused by the patient

The disease, the etiology of which is obscure, occurs chiefly in many cases of the disease is due to the perversion of the internal secretion of the thyroid gland which is increased in quantity and also acquires certain toxic properties

Gamma rays of radium irradiation often prove most beneficial especially if there is no vomiting or diarrhoea and the patient is not much emaciated

Flat applicators are employed and Gamma radiation given in treating the thyroid gland. The cellular secretion of the thyroid becomes normal and the gland becomes smaller on account of the fibrosis caused by the radium exposure

Radium therapy is of but little value in cases of parenchymatous, cystic and adenomatous goitres and so these cases should be treated surgically

#### BENIGN TONSIL LESIONS

Surgical removal is a treatment of choice but if operation is not feasible or is refused by the patient, such cases can be satisfactorily treated with radium. X-rays also can be used but radium is preferable in cases of children who do not keep steady while x-ray exposure is being given

Chronically infected tonsils are usually hypertrophied. The enlargement is due to an increase in lymphoid tissue, engorgement of the tonsillar crypts and general chronic inflammatory swelling

The lymphatic tissue in chronic hypertrophied tonsil is especially susceptible to the rays of radium. Atrophy of the lymphoid tissue in tonsil is brought about by radium rays. The inflammatory process disappears and fibrous tissue is formed

Radium flat applicator containing from 20 to 30 mgs of radium should be prepared. A filter of 0.6 mm of platinum and 1 mm of silver is employed to cut off all rays except Gamma rays. Each sitting is of 2 to 3 hours according to enlargement of the tonsils and age of the patient. It is applied externally on the neck below the angle of the jaw and the rays are directed towards the tonsil

Deep external irradiation should not cause a local inflammatory reaction but only a gradual shrinkage of the susceptible lymphoid tonsillar tissue

#### KELOID

Keloid is a dense fibrous growth of the corium usually



in the scars of injuries but occasionally occurring spontaneously It presents as a raised firm pink or red mass of irregular outline Microscopical examination shows them to be composed of interlacing bundles of collagen which frequently exhibit an almost hyaline structure They are further characterised by an increase in the cellular and vascular elements True fibroblasts are but few in number

Excision alone is particularly useless, the keloid almost invariably recurring in the operative scar Good results may be obtained by excising the keloid and subjecting the operation area to radium irradiation directly when the incisions have healed

Exposures to Gamma radiation gives satisfactory results A flat applicator is prepared sufficient to cover the operation scar and exposures of 3 hours every day for 3 successive days are given Three months are allowed to pass and then again radium exposure given if necessary If operation is not performed for any reason then radium exposures should be given It takes more time but in the end results are good Little or no reaction follows upon this treatment which induces a slow but steady absorption of the keloid mass and a gradual restoration of the colour to normal

### REMARKS

by Dr K. P. MODY

Commenting on Dr Joshi's paper Dr K P Mody said that Dr Joshi had done well to draw attention to the great value of radiation treatment to non-malignant conditions He regretted that Dr Joshi had spoken about the uses of radium in such conditions as Tb glands, uterine bleedings, hyperthyroidism, spring catarrh and other eye conditions, as x-ray treatment could be used with equal success in these cases and with greater ease and convenience and with greater precision He complimented Dr Athle for his lucid and instructive address on x-ray diagnosis in bone tumors Considering the great difficulties in diagnosis Dr Mody felt that it was imperative that Bombay should maintain a registry of bone tumors on the same lines as the U.S.A He further suggested that not only diagnosis but also treatment of these cases should be centralised in one place, so that at the end of 5 or 10 years there would be a wealth of material available to the great benefit of the patients and to the scientific world

He felt that the value of x-ray treatment was not sufficiently realised in acute inflammations Simple conditions like boils, serious lesions like carbuncles and grave entities like erysipelas and cellulitis reacted very favourably to a few small doses of x-ray, 3 to 5 sittings being all that was required to bring about resolution and localise the lesions He referred to that dreadful complication in military surgery, gas gangrene He himself had no personal experience of the condition but he quoted statistics compiled by Kelley in America X-ray treatment was the treatment of choice and the best results were obtained when x-rays were used alone, the mortality rate being as low as 5 per cent Septic peritonitis, a serious problem in the battle-

(Continued on page 163)

# The Indian Physician

VOL III NO 6

JUNE, 1944

WHOLE NO 30

## Original Contributions

### ASPIRATION BIOPSY IN THE DIAGNOSIS OF MALIGNANT TUMORS

by

V R KHANOLKAR

AND

V V GHARPURE

(From TATA MEMORIAL HOSPITAL, BOMBAY)

*"The age calls for simple statements  
and restatement of simple truths"*

LIN YUTANG *Preface to Myself*

It is now generally accepted that a rational treatment of any neoplastic condition could only be based on an accurate diagnosis of the lesion. When the neoplastic process has advanced beyond a certain stage its clinical recognition offers hardly any difficulty. In the early stages when the physical signs with which most medical men are familiar are not evident, the diagnosis is attended with considerable uncertainty. Unfortunately, it is in the early and curable cases that an accurate diagnosis becomes important and a clinician could ill afford to neglect any technique which may assist him in arriving at a decision, with promptitude, precision and accuracy.

A carefully recorded history and a thorough painstaking clinical examination supplies the basis for all diagnosis. The radiological investigation adds valuable information, but the ultimate opinion in most cases rests on the histological findings in a piece of tissue removed from the tumor. The prevailing ideas regarding the indications of a biopsy are unfortunately very nebulous and the opinions of many medical men regarding what may be expected from a biopsy are quaint and naive. It is generally believed that a biopsy is unnecessary when a clinical diagnosis could be reached without its assistance. It is thought that the taking of a biopsy is purely a matter of "academic

interest" and may find some use, if at all, in hospital records. It is further bruited about, that a biopsy is attended with definite danger to the patient and tends to aggravate the local extension of the disease, or at any rate to expedite its rapid dissemination. A voluminous literature has accumulated on this subject but it is scattered over many specialised journals and almost all of it in foreign countries. It may, therefore, be opportune to review briefly our own experience with biopsies particularly with aspiration biopsy which is being practised by us for the last three years.

Although a clinical examination of the patient affords the basis for diagnosis, it is liable to serious errors in the case of malignant tumors. These may be due to the fact that the examining physician is not actively and constantly in touch with problems of malignant disease. They may be eliminated by experience and systematic study. It has, however, been found that even with the most experienced observers such errors continue to recur unless supplemented by a routine biopsy examination. A few examples may clear any doubts that may be entertained in this respect. Over 50 years ago Ruge (32) in Berlin showed that 13 out of 23 cervixes that had been amputated for early cancer were not cancerous. In the case of breast tumors Halstead and Bloodgood (5) both masters of clinical diagnosis in their time, working together in Baltimore had incorrectly diagnosed 54 out of 542 tumors. In a recent study Borges (7) at the Tata Memorial Hospital reported a mistaken diagnosis on 13 in 158 cases of breast disease which was corrected by frozen section examination at the time of operation. In 105 bone tumors, Troell (39) found that one out of every four cases in the hospitals of Stockholm were wrongly registered as sarcoma. MacCarty (22) in a study of 1213 surgical cases at the Mayo Clinic found that in 17.5 per cent the histological diagnosis changed the operative treatment and prognosis. W. Fischer (14) found the clinical diagnosis to be correct only in 68 per cent of the 1700 surgical specimens removed for cancer. Rich (31) has reported that in 292 consecutive autopsies in men over fifty at the Johns Hopkins Hospital, 14 per cent showed a carcinoma of the prostate and that in 65 per cent of these a diagnosis of cancer had not been made during the life-time of the patient. In most of these studies it was shown that a microscopical examination of the tumor tissue reduced the mistakes in diagnosis from about

30 per cent and less, to 10 per cent and less. In view of these findings the opinion expressed by Regaud (30) deserves careful consideration. He thinks that histological examination formed at present an essential part of the treatment of cancer. "For the patient, it is an indispensable step which he has a right to expect, for the physician, it is no longer a manifestation of his scientific curiosity, but an obligation."

A biopsy enables the attending physician to decide upon the appropriate type of treatment because the choice of surgery or radiation in the therapy of tumors hinges largely on an exact knowledge of the neoplastic cells which make up the tumor. Experience of the last 20 years has shown certain types of tumors to be highly radiosensitive and others in the same region very resistant to such therapy. A consideration which is lightly brushed aside by many people is the exactitude of case records. In several institutions visited by us we have been surprised by unreasonable claims regarding the efficacy of some pet type of treatment which has found an ardent advocate. It should be obvious that no claims deserve serious notice unless it is known that the original lesion was a histologically proved malignant tumor and the patient had been under observation for a stated interval of time. It is astonishing that a local regression and the ability of a patient to survive a treatment is often accepted as an evidence of a cure in many clinics.

It is necessary for the physician to be acquainted with the limitations of histological diagnosis to obtain the greatest benefit for his patients, and to realise exactly how much to expect from this particular technique. In common with most other laboratory investigations a positive diagnosis has an incomparably greater value than a negative report. Errors in positive diagnosis are almost always due to poor technique, insufficient training and an inability to interpret correctly the microscopic picture. Negative reports are rarely referable to the skill and competence of the pathologist. The person working in the laboratory can only report on the material he gets and the diagnosis depends on the operator's ability to obtain representative tissue from the suspected lesion. It is regrettable that sometimes a clinician looks upon microscopic diagnosis as a trial of wits between the pathologist and himself. It is our growing conviction that the reliability of histological diagnosis is very often

determined by a close co-operation between the surgeon and the pathologist "The probable clinical impression and the location, size, duration, rate of growth and general physical features of the tumor should always form the background for a pathological diagnosis" Ewing (12) The histological diagnosis of tumors is a difficult subject and should not be lightly undertaken by people who probably see a dozen preparations during the year The interpretation of microscopic sections in many instances is simple, but a correct reading in most cases is a matter of visual memory, specialised training and continuous operation in a well organised laboratory It is not sufficiently realised that the difficulties of histological diagnosis become insurmountable if the biopsy material is obtained by blunt instruments, if it is squeezed, crushed or torn by dissecting and other forceps or deeply coagulated by electrocautery The drying of tissues wrapped or exposed on gauze or lint and the crushing by instruments produce nuclear changes and cytoplasmic distortions which militate against any attempts at a reasoned judgment on the microscopic appearances It is necessary to state that in a certain small proportion of cases the nature of the pathological lesion does not admit of any definite expression of opinion "A lesion may be neither cancer, nor not cancer It may be in the process of becoming cancer" Ewing (12) It should also be pointed out that in certain types of tumors like some papillomas, adenomas of thyroid, few lymphosarcomas and cellular fibromas the biological behaviour of the tumors rather than its microscopic structure affords the more reliable indications of its nature

#### DANGERS OF BIOPSY

The exploratory incision into a deep seated neoplastic lesion is decidedly dangerous to the patient in untrained hands We had occasion to observe repeatedly a fungation and infection of tumor tissue, its ulceration and rapid spread after a careless cutting into tumors of breast and bone These dangers are completely removed by a careful attention to technical details If precautions are taken to ensure rapid healing of the wound, by employing a small incision, meticulous hemostasis, avoidance of sharp retractors, by gentle handling of tissues and careful suturing of connective tissue capsule, the removal of tissue for biopsy is never followed by adverse effects As there is still a lurking suspicion in the minds of many people regarding the

dangers of biopsy even in skilled hands it is necessary to review some recent data in this connection. This information is available both from clinical observations and from experimental studies on animals. In the case of 38 patients who had been treated for cancer of the cervix and had remained well for many years after operation, Martzloff (27) found that 36.8 per cent had been subjected to a diagnostic curettage several days prior to operation. He therefore believed that curettage had not affected the chances of recovery in his patients. In a recent study on the influence of incisional biopsy either before or at the time of operation on the results of radical mastectomy, Haagensen and Stout (19) from the Presbyterian Hospital, New York, found the five year clinical cures to be 49 per cent with biopsy as against 34 per cent without biopsy. The Coleys (9) with their large experience of bone tumors have not come across any adverse effects following aspiration biopsy in such tumors. As regards the experimental evidence, the often quoted observations of Francis Carter Wood (40) deserve restatement. He inoculated 400 rats of a known strain with Flexner rat carcinoma, which under normal conditions leads to lung metastases in about a fifth of the number of the experimented animals. After successful implantation he separated a group of animals in which he removed a slice of tumor tissue. The proportion of animals, who developed secondary deposits in the lungs after a certain interval of time, was practically the same in biopsied and in control animals. McLean and Sugiura (28) after repeated aspiration biopsies in transplanted rat carcinoma and mouse sarcoma did not produce any noticeable damage to the tumor capsule. There was no increase in the number of animals showing distant metastases, nor was there any implantation along the track of the aspirating needle. Haagensen (18) has pointed out that it is doubtful if these findings could be made applicable to human material, as the mode of spread of these animal tumors is different from the usual types of human cancer.

#### METHODS

The material for histological examination is obtained by a punch, or cut out by a wedge shaped incision or a semicircular swoop with a knife, or removed through a hollow needle. The method to be adopted depends on the site of the tumor and its supposed pathological nature. It is the usual practice to use a punch forceps whenever the exposed tumor could be

visualised naked eye or through a suitable tubular instrument e.g., bronchoscope, cystoscope etc. In the tumors which lie under the skin or mucous surfaces but could be easily reached, an incisional biopsy is usually simple and best suited for histological examination. The method of obtaining material through a hollow needle is being used extensively during the last ten years. Owing to the fact that it leads to very little traumatisation and is fairly simple to carry out, it presents distinct advantages in certain types of tumors. The material obtained by this method is either smeared on glass slides, or bits of tissue are fixed and sectioned in the usual way. The aspiration smear method was described by Martin and Ellis (24) and is mainly used at the Memorial Hospital in New York. The ease of operation and the rapidity of diagnosis have favoured its adoption in many surgical clinics. It should, therefore, be pointed out that there are some definite limitations which should be clearly realised by all who wish to employ this method of diagnosis. It has been used in selected cases at the Tata Memorial Hospital since its commencement and it is intended to present the result of our experience with it.

(1) It is evident that the chances of failure with this method would be great if the lesion happens to be small and deep seated, because of the lesser likelihood of impinging exactly on the suspected neoplasm.

(2) The usual architecture of the tumor tissue is invariably distorted and lost by the mechanical stresses involved in aspiration and smearing of the material.

(3) The most that could be expected from an examination of the smears would be to determine correctly whether tumor cells were present at a suspected location and whether they were epithelial or non-epithelial in origin. It is not possible to estimate the degree of differentiation of tumor cells nor to adjudge the grade of malignancy.

In no other type of biopsy examination is the diagnosis so dependent on the clinical background of the tumor. "Knowing the source, knowing what tumors are apt to occur in the region and being fully cognisant of the histological criteria for the diagnosis of such tumors from ordinary sections, one may form from the various minutae of the smear, a sort of composite picture which permits a visualisation of the probable histology of the process and hence a diagnosis of the type of tumor."

Martin and Ellis (26) We, therefore believe that this type of histological examination could be undertaken with confidence only in those institutions where the co-operation between the clinician and the pathologist is complete and where the pathologist has uninterrupted opportunities of familiarising himself with fine microscopic details in sections and smears

#### TECHNIQUE

It is unnecessary to repeat the technical details of aspirating tumors which have been thoroughly described in publications which have appeared in the last 13 years (1, 2, 3, 8, 9, 10, 11, 15, 23, 25, 33, 36) The method employed by us differs in no essential respects from that of Martin and Ellis The few modifications which have been employed successfully by us may be mentioned

(1) The cellular details are invariably damaged by drying We, therefore, immerse the slide immediately after smearing in a fixing fluid We should like to emphasise the fact that in preparing the smear, the application of as much pressure as the slide can easily withstand is essential for success

(2) We are partial to formol-corrosive fixative, which is prepared by adding 10 parts of formaline (40 per cent formaldehyde solution) to 90 parts of a 5 per cent aqueous solution of mercuric chloride The time for fixation is from 5-30 minutes

(3) We suggest that the method of staining should be the one with which the person employing it is most familiar Ehrlich's haematoxyline followed by watery 0.5 per cent Eosin Y solution has yielded us consistently good results

#### INTERPRETATION

In properly prepared slides the tumor cells appear in coherent groups or sheets which are fairly evenly distributed in the smeared area The carcinoma cells can usually be distinguished from sarcoma cells The former are generally larger, more polygonal and exhibit a high degree of polymorphism The variation in size of individual cells may be marked and very large tumor cells or giant cells may be encountered The nuclei of these cells show the most characteristic changes An increased nuclear activity is suggested by clumping of the chromatin, granularity of the nucleus and an apparent augmentation of the nuclear material Cells are sometimes seen in the process of mitotic and amitotic division The most frequent variation of the nucleus is in its size In carcinoma



the nucleus is irregularly situated and often fills the entire cell, leaving a thin but distinct rim of cytoplasm. In some tumors the large nuclei are matched by an equally wide cytoplasmic fringe. Nucleoli are seen but not consistently enough to aid in diagnosis. The staining characters of the cytoplasm are variable and may vary from basophilia to a distinct oxyphilic reaction. The material from one type of enlarged neck nodes frequently encountered by us shows large polygonal cells held together in groups or loosely scattered in the smear. The cells have abundant acidophilic cytoplasm with round or oval pale nuclei. The nuclei vary markedly in size and shape. Few cell groups of the usual hyperchromatic type are interspersed between these cells. Flakes of amorphous, acid staining material and large monstrous cells are also seen. We associate these characters with degenerating epidermoid carcinoma. The sarcoma cells are usually smaller, more uniform in size, and contain remarkably spindle shaped nuclei in the fibro-sarcoma type of tumors. The nuclei are usually paler, with minute nucleoli when present. In the lymphosarcoma the nuclei are round and the cells resemble those seen in blood films containing lymphocytes and lymphoblasts. Tischendorf (38) has described individual traits, which he utilises for the diagnosis of different kinds of tumors. Our experience does not encourage us to go beyond the group characters mentioned above and we prefer a formal biopsy for a more detailed histological study if it could be obtained without detriment to the patient. In smears from benign epithelial tumors adherent sheets of small polygonal cells are seen. The cells have well defined outlines and a uniformly staining cytoplasm. The nuclei are small, regular and centrally situated in most tumors.

## RESULTS

In the first 5,000 consecutive cases which were examined at the Tata Memorial Hospital during the last 3 years, it was found that 3,643 presented neoplastic lesions, and in the remaining 1,357 no such lesion could be detected. Aspiration biopsy was carried out in 675 cases to assist in this sorting out of disease conditions. Out of 675 patients the biopsy had to be repeated one or more times in 207 patients before the fact of malignancy could be established. We agree with the view of Martin and Ellis (26) that "no one with wide experience in the diagnosis and treatment of cancer will implicitly rely on one negative biopsy,



Fig 1—Malignant tumor of the frontal sinus (#6383) in a 53 year old woman.

Fig 2—A formal biopsy of a preauricular node from the same case taken by an inexperienced surgeon, shows marked cytoplasmic distortion and a crushing of nuclei making it impossible to give a histological diagnosis of the tissue.  $\times 150$

Fig 3—A formal biopsy from another preauricular node from the same patient taken later by an experienced surgeon enabling a diagnosis of transitional cell carcinoma of a low grade of differentiation.  $\times 150$

Fig 4—Aspiration biopsy smear from a degenerating epidermoid carcinoma (#5016) showing flake of amorphous acid staining material with monstrous cells—large polygonal cells with round or oval pale nuclei and abundant acidophilic cytoplasm.  $\times 300$

KHANOLKAR AND GHARPURE—ASPIRATION BIOPSY

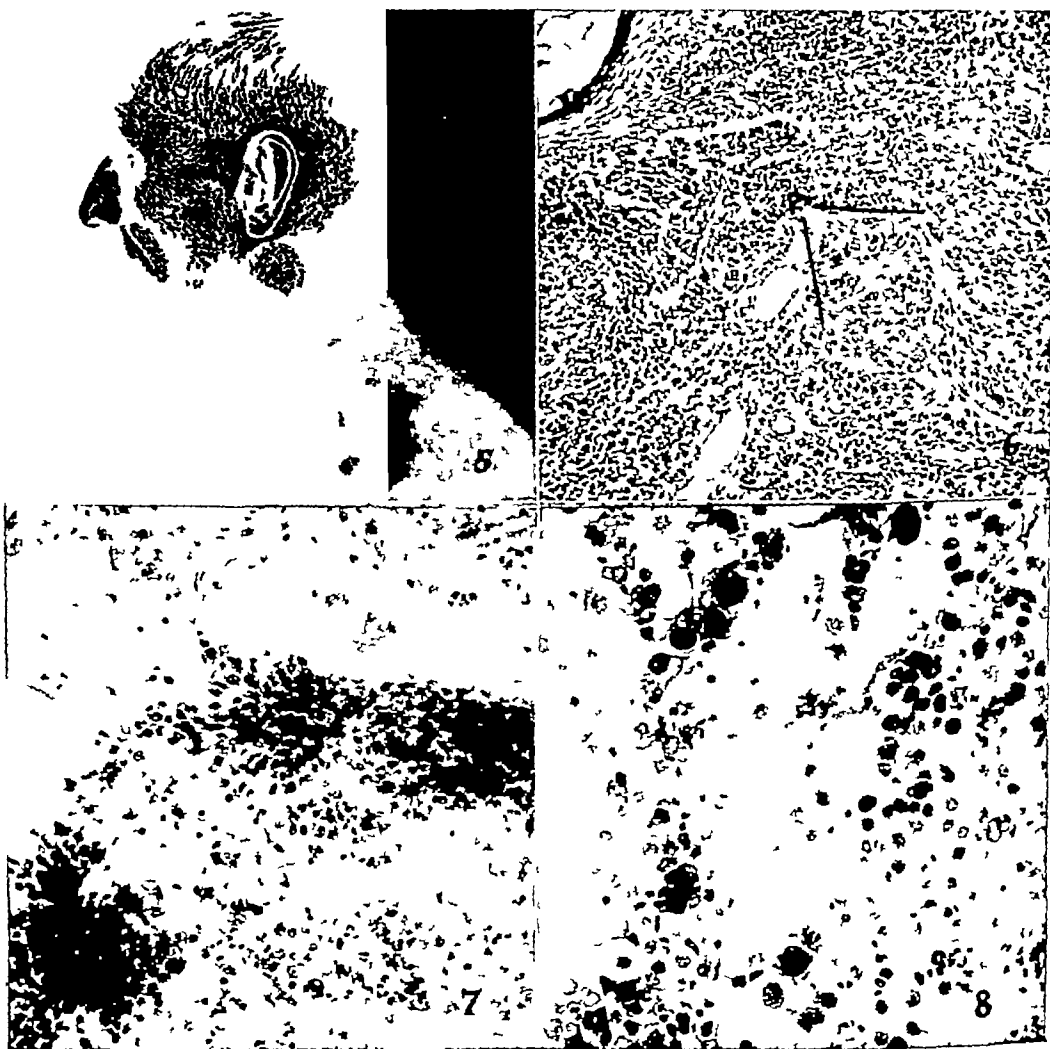


Fig 5—Enlarged cervical glands with a small primary lesion at the base of the tongue ( $\pm 1018$ ) in a man aged 40 years

Fig 6—Punch biopsy from the primary lesion showing the histological characters of an epidermoid carcinoma. (A) cords of tumor cells lying in the subepithelial tissue  $\times 150$

Fig 7—Aspiration biopsy smear from the neck node (low power) showing tumor cells scattered about as well as clumped in three large groups  $\times 150$

Fig 8—Aspiration biopsy smear from the neck node (high power) The nuclear characters with variations in size and situation as well as the granularity of the chromatin material are well shown  $\times 300$

whether by aspiration or incision, if this histological report be inconsistent with clinical findings" Majority of patients who seek admission are found to be suffering from disease in the head and neck region. Out of 3,263 patients with malignant disease 1,041 had evidence of oral cancer and 323 of cancer in the vicinity of the larynx. The method of aspiration biopsy, therefore, found its largest scope in our clinic in the case of enlarged neck nodes following metastatic involvement or owing to primary disease. Out of a total of 654 this technique was employed in 505 patients with some type of enlargement of neck nodes. The accompanying table (I) shows the nature of the lesion and the number of patients in which it was possible to diagnose malignant disease by an examination of the aspirated material.

TABLE I

The results of the Aspiration Biopsies performed on ENLARGED NECK NODES  
in 505 cases (1 — 5000)

Clinical diagnosis of the primary lesion	Total no of cases	Number of cases in which aspiration biopsy was performed	No of cases in which a diagnosis of malignancy was reported on smears	No of cases where a formal or a punch biopsy on the primary was reported malignant	No of cases where the smear diagnosis was confirmed by a histological section of		
					Clot	Formal Biopsy	Autopsy
Ca. Buccal mucosa	170	32	10	29	4	2	—
Ca. Tongue Ant 2/3	101	14	11	11	—	1	—
Ca. Palate	66	11	7	7	2	—	—
Ca. Tonsil	182	49	38	32	3	—	1
Ca. Base tongue & pharynx	439	128	90	89	11	6	—
Ca. Nasopharynx	22	9	7	6	—	—	1
Ca. Larynx	323	127	91	61	8	4	—
Primary not detected	60	60	56	—	5	8	—
**Malignant lymphomas	40	16	11	9	1	9	1
Ca. Maxillary sinus	34	3	3	2	1	1	—
Malignant tumors mediastinum	7	5	2	3	1	—	—
Ca. Lung	23	4	4	—	—	1	—
Ca. Urinary bladder	7	1	—	1	—	—	—
Ca. Cervix	293	1	—	1	—	—	—
Chronic inflammatory and tubercular neck nodes	92	47	—	—	3	5	—
<b>TOTAL</b>	<b>1871</b>	<b>505</b>	<b>336</b>	<b>251</b>	<b>39</b>	<b>37</b>	<b>3</b>

\*\* This term is used in a wider sense as adopted by Gall and Mallory (17)

In a recent study of 3896 cases in the head and neck services at the Memorial Hospital, New York, Martin and Morfit (26a) found that 218 patients presented themselves with an initial and only complaint of visible, palpable cervical tumor, with silent primary malignant disease. In 55 of these no primary cancer was discovered either up to the time of death or after at least a five-year period of observation. In all these cases the

enlargement of cervical lymph nodes was shown histologically to be due to either a squamous or an epidermoid carcinoma

We would particularly like to direct the attention to a group of 60 cases in which a careful clinical search failed to reveal a lesion in the mouth, nose and throat and yet the lymph nodes showed an involvement by an epithelial type of tumor. The tumors belong to the class of debatable tumors about which we do not think that either we or anyone else, would at present be qualified to give a final opinion. We believe that most of them belonged to the group of radiosensitive tumors described as lymphoepithelioma by Regaud and by Schminke (34), "in which the lymphoid tissue is intimately associated with an immature squamous or epidermoid type of malignant epithelium" Harvey, Dawson & Innes (20). It seems that such tumors are fairly common amongst the Malays and the Chinese. Bonne (6) has pointed out that "the pathologist in the Far East acquires more experience with these tumors in a few years than do his Western colleagues in a life time". Bercovitz (6a) reports that cancerous enlargement of the glands of the neck is the most frequent form of malignant disease encountered in the Presbyterian Mission Hospitals in Hainan, China. It accounts for 21.61 per cent of their cases of malignant disease, occurs usually in people under 40 years of age and presents a problem regarding the location of primary disease in the majority of cases. The lesion is diagnosed microscopically either as "lympho-endothelioma," lymphosarcoma or metastatic carcinoma. He further states that "Inquiry from several sources has indicated that cancer of the glands of the neck is not seen commonly north of Canton and Hongkong". The disease appears to be less frequent in these two places than in Hainan.

In another group of 47 patients the clinical diagnosis was uncertain regarding the nature of the enlargement but was shown to be of a chronic inflammatory origin. We believe that they were tubercular, though in only one instance we were able to demonstrate acid and alcohol fast bacteria in the aspirated material. No attempt was made to identify the organism by culture on suitable nutrient media. In eight instances where the clot or a formal biopsy was available the microscopical appearance was indicative of tuberculous lymphadenitis.

The results of aspiration biopsy from sites other than neck nodes are shown in table II. Three groups deserve further

scrutiny The method has been particularly useful in the case of lung tumors, specially those which were not easily accessible to a bronchoscopic biopsy In 11 out of 15 patients it was possible to report the presence of a malignant tumor on an

TABLE II

The results of the Aspiration biopsies performed on sites other than neck nodes

Site of Aspiration biopsy	Total no of cases	No of cases aspirated for biopsy	No of cases in which a diagnosis of malignancy was reported on smears	Number of cases in which the smear diagnosis was confirmed by a histological section of		
				Clot	Formal Biopsy	Autopsy Tissue
Orbit	22	8	2	3	2	—
Maxillary antrum	34	9	7	4	4	—
Palate	66	1	1	—	1	—
Parotid tumors	22	16	8	—	8	—
Thyroid swellings	19	7	5	2	2	—
Lung tumors	23	15	11	6	1	—
Breast tumors	166	26	18	5	8	1
Soft tissues	65	29	9	5	9	1
Axillary and inguinal lymph nodes	17	13	8	2	2	—
Prostate	7	4	2	1	—	—
Liver	4	4	4	1	—	1
Spleen	1	1	—	—	—	—
Testis	44	1	1	—	1	—
Bones	30	20	10	10	6	2
TOTAL	520	149	86	39	44	5

examination of the smears Craver and Binkley (10) from the Memorial Hospital, New York, have reported positive findings in 60.8 per cent of aspiration biopsies in lung cancers Blady (4) has described the technique of aspirating deeply situated tumors in the vicinity of vital structures under roentgenoscopic guidance The method was tried at this hospital successfully in some cases

In the case of thyroid tumors Fred Stewart (36) after a long experience in this technique is of opinion that it is difficult to differentiate between benign hyperplasia and low grade cancer, and recommends caution in diagnosis of malignancy on the basis of aspiration smears In our material it was possible to diagnose malignancy in 5 out of 7 cancer thyroid patients, but this may have been due to the marked anaplasia of the tumor cells in all these cases In bone tumors the method promises definite advantages and has been recommended by Ewing and by Coley (9, 11) A modification of the usual technique is being developed and the results will be published separately

#### DISCUSSION OF RESULTS

Out of 505 cases of enlarged neck nodes in which aspiration biopsy was performed malignancy was reported in 336 patients, and in 47 cases a diagnosis of chronic inflammatory condition was made The correctness of these reports in 381 cases is borne out by the subsequent clinical course of disease in the patients In the group of aspiration biopsy in other regions malignancy was

reported in 86 out of 149 cases. The negative reports in 169 cases in the neck nodes and 63 from other regions may have been due to an absence of neoplastic condition or because tumor material was not aspirated. A negative diagnosis, therefore, should not be construed as an erroneous report. In three instances a wrong positive diagnosis was made and these cases in view of some instructive features deserve a fuller description.

**Case 135** An aspiration biopsy was performed on a swelling in the parotid region. A diagnosis of malignancy was reported on the basis of a single group of squamous cells on the assumption that the smear was made from the material obtained from a lymph node. After the operative removal a diagnosis of tuberculous lymphadenitis involving the parotid gland was made. The single group of squamous cells was probably an inclusion of skin epithelium in the material. A contamination of this type could be avoided by making a snik with a knife in the skin before inserting the needle. A diagnosis of malignancy should never have been made on the basis of a single group of cells.

**Case 1365** A middle aged woman had an oval tumor mass situated over right dome of the diaphragm at the base of the lung. The aspiration biopsy was reported as a low grade connective tissue malignant tumor. This patient is still alive after two years without any spread of the disease or metastasis. On reviewing these smears the cells are seen to be small, spindle shaped and loosely arranged, the nuclei are small, ovoid and regular in size and shape. A diagnosis of malignancy should not have been made on these smears.

**Case 77** A large shadow in the lung clinically and radiographically diagnosed as dermoid of the lung, in a middle aged man. An aspiration biopsy was performed and the smears showed acidophilic acellular material. It was reported as being consistent with the diagnosis of a dermoid. After an autopsy there was seen a large tumor mass occupying practically three-fourths of the right lung. The cut surface showed a yellowish, greasy mass with a thin ring of tumor tissue. Histological sections showed it to be an epidermoid carcinoma, grade 3, with large areas of central necrosis. The material in the smears was probably derived from these degenerated areas.

Since the histological diagnosis depends not only on the types of cells but also on the relation of the cells to each other,

no clear idea of the general structure and cellular orientation could be obtained by aspiration smears. The method is therefore unreliable for grading and classification of tumors. Attempts have therefore been made to obtain a cylindrical plug of tissue through a needle by different devices (15, 21, 35, 37, 41). One of us (VRK) has seen excellent preparations from tissue removed with Silverman needle at the State Institute for the study of malignant disease in Buffalo, USA. A cylinder of tissue about 2 x 10mm is obtained which is fixed, embedded and sectioned, and is usually sufficient for diagnosis of tumors in most cases. The advantages of the method are obvious, but our personal experience is too restricted to be of much value so far. Recently it has been recommended for obtaining biopsies from suspected disease of the prostate by Pearson and Nickerson (29).

#### SUMMARY AND CONCLUSIONS

Results of aspiration biopsies performed at the Tata Memorial Hospital during the first three years are discussed. The indications and contraindications of biopsies for diagnosis of malignant disease are reviewed. It is suggested that this technique should not be undertaken by those who have inadequate facilities for continued practice in the interpretation of such material.

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# THE ROLE OF ANAEROBIC STREPTOCOCCI

## DURING PREGNANCY, LABOUR AND THE PUERPERIUM WITH THE RESULTS OF INVESTIGATIONS ON THAT PROBLEM

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The aim of my paper is to present the results of investigations on the role of anaerobic streptococci during pregnancy, labour and the puerperium, which I had the privilege to carry out in the Pathology department of G S Medical College during the period of two years and half. The problem occurred to me on noticing in the private practice some amount of morbidity amongst the normally delivered cases which called for no P V examination nor any operative manipulation during labour. I will limit myself to the end results of the various investigations. But before I present the figures and the statistics, may I take this opportunity to discuss in short the present available literature on the problem of the role of anaerobic streptococci during pregnancy, labour and the puerperium and the current theories as regards its relation to the genital infection.

The genital infection in the puerperium still tops the list of the causes of maternal mortality after labour in spite of the recent advances made in the science of obstetrics. The actual mortality rate has no doubt come down to some extent as can be noticed from the figures by various authors.

TABLE 1

Maternal Mortality	Death due to Sepsis
Dublin in 1918	47% of the total death
Woodbury, 1921	40%
Frankel 1924	37.7%
Vital statistics from the Dept of Commerce	
U S A in 1933	37%
Dr Miss Jhirad in report of maternal mortality in the city of Bombay in 1937	39%

The actual incidence of death from sepsis is also greatly reduced with the advances in the surgical antiseptic method of delivery. Before the antiseptic era the maternal mortality due to sepsis was 10-15 per cent as noted in "The old maternity of Paris" and "Lying in Hospital in Vienna". In 1929 Howard who brought forward the figure of 27 per cent incidence of puerperal sepsis, quotes that one in every 406 pregnant women die of infection, i.e. incidence of 0.25 per cent while Pinard the great obstetrician of his day obtained an incidence of 0.15 per cent in 45,633 deliveries conducted with his utmost conservative doctrines. The Vital Statistics of Department of Commerce formed in 1933 the death rate due to puerperal as 0.24 per cent, i.e. 2.4

per thousand live births In India due to the defective birth requisition system, this figure is usually found very high as all the deaths are registered but not all the births Dr Miss Jhirad in her report has given the figure for the City of Bombay for 1937 as high as 8.9 per thousand live births, although the figures for the previous years as given by the Director of Public Health, Bombay Presidency and by the Executive Health Officer of Bombay as 4.2 per thousand births and 4.4 per thousand respectively The figures for England and Wales are only 3.5 per thousand live births

TABLE 2  
Mortality in Pregnant Women due to Sepsis

Paris maternity & Vienna Hospital	10.15%	
Howard—1929	0.25%	
Pinard—1909	0.15%	
Vital Statistics—1933	0.24%	Death from puerperal septicaemia
Miss Jhirad for Bombay—1937	0.89%	
Director of Public Health, Bombay Presidency—1936	0.42%	
Executive Health Officer, Bombay—1936	0.44%	
England & Wales	0.35%	

With the recent advances made by the discovery of sulfanilamide group of drugs the mortality figures are still further reduced as can be noted from the report of the New York lying in Hospital in 1939 The figure quoted is only 0.03 per cent

Colebrook, Kene & Purdie from the Statistical Study of the cases of puerperal sepsis treated with prontosil and sulfanilamide showed definite decrease in the mortality figure in cases of  $\beta$  haemolytic streptococcal infection They found a drop in the figures from 22 to 8 per cent in very severe and fulminating type of septic cases

Thus a fall in the mortality figures in septic cases produced by haemolytic aerobic streptococci can be obtained by the use of sulfanilamide in suitable cases and also by observing certain strict routines during the conduct of labour so as to avoid the extrinsic infection These are chiefly the careful use of mask during labour both by the nurses and doctors and even by patients if possible, the observance of the usual surgical aseptic and antiseptic procedure during confinement, the limitation of P. V. examination and the internal manipulations to a minimum, the maintenance of the labour room as free from dust and infection as possible and the confinement of septic cases or the cases with fever in a separate room and preferably conducted by a separate staff

With all these precautions, even though the mortality figures can be reduced to a great extent, a certain amount of mortality and a good bit of morbidity still persists in the obstetric practice In New York Hospital to which a reference was just now made, morbid puerperia were noticed in 10.54 per cent of the delivered cases These 10 per cent were formed by the genital infection proper in 8 per cent and while in the rest 2 per cent the infection was present in the other systems in the body

TABLE 3  
Taken from Dr Miss Jhirad's Report.  
Incidence of morbidity 11%  
40.6% after normal delivery  
59.4% after complicated and instrumental labours.

The morbidity at three large centres in Bombay as reported by Dr Miss Jhirad averaged 11 per cent of their total deliveries. Of these 40 per cent were after normal deliveries and the remaining 59.4 per cent occurred after complicated instrumental and other deliveries. It will be evident that this second figure can be reduced by means of various measures detailed just now. But the other figure, namely 40 per cent cannot be appreciably reduced in spite of all our present-day advances. The persistence of this morbidity in this group of cases, i.e. cases with endogenous infection is due to the fact that the sulfanilamide is found to have bacteriostatic action on the  $\beta$  haemolytic streptococci only and is useless in anaerobic streptococcal infection. The latter organisms are the normal inhabitants of the vagina of pregnant women and their incidence varies according to the social status of the individual.

It is no wonder, therefore, that the different investigators working with the different classes of patients obtained a varied figure as regards the incidence of these organisms. There is one more additional factor, namely the climate of the country which may affect to some extent. This was the problem one had to deal with first so as to find out the figures for our Indian patients.

TABIE 4  
Anaerobic Streptococci in Pregnancy

Natwig (1905)	5/10 cases	50%
Wegetius (1909)	7/10	70%
Rokowsky (1912)	65 cases	40%
Soule & Brown (1932)	207 cases	39.5%
Elizabeth White (1933)	50 cases	30% Strict Anaerobes
Colebrook & Hare		40%
Figures in this investigation		
Anaerobic streptococci		54%
Strict anaerobic		16%

Natwig in 1905 found them present in 5 out of ten cases examined during the first stage of labour. Wegetius in 1909 found them in seven out of the ten patients during the same stage. Rokowsky in 1912 using plate cultures over pyrogallol isolated anaerobic streptococci in 40 per cent of a group of 65 normal women. Soule & Brown in 1932, using blood agar slopes and minced meat medium got 39.5 per cent positive obligatory anaerobic streptococci cases in their investigation in 207 pregnant women. But these were the results long before the present improved method of growth of anaerobic streptococci was known and the investigators did not work to distinguish between the strict anaerobes and the facultative aerobes. Comparatively recent systematic investigation was carried out by Elizabeth White in 1933 and she found anaerobic streptococci present in 30 per cent of 50 cases examined during the last month of pregnancy.

In short the incidence of anaerobic streptococci depends on the type of patients examined and the method used for the isolation of the organisms. In John Hopkin's Institute it was noticed that the incidence of the febrile puerperium varies materially with the social status of the individual patient although all of them may be delivered by the same staff, in the same delivery room and by the same routine. In 5514 ward patients 26 per cent of the negroes had a rise of tem-

perature to  $100.4^{\circ}$  on two or more days of the puerperium as contrasted with 14.4 per cent of the white patients, the ratio being one to two. This fact supported strongly that the different vaginal flora in the different group of patients was capable of high incidence of puerperal infection in the lower social class of patients.

The other factors which favour the infection by the anaerobic type of organisms in addition to the one so far dealt with, are the history of prolonged labour, the premature rupture of membranes, the presence of marked tissue damage, the latter being the most important among them all as will be evident when I discuss the morbid pathology in this type of infection.

When any of these factors exist, it is possible to develop auto-infection in patients who harbour these potentially pathogenic organisms, like anaerobic streptococci. The same idea was expressed by the great obstetrician Semmelweis who stated that in rare instances the decomposed animal material, which causes the child birth fever when absorbed, is produced within the patient herself. These are the cases of auto-infection which cannot be prevented. Little must have Semmelweis then realised that the statement had any bacteriological backing to prove it as we can clearly see it now.

Anaerobic streptococci have been missed as the causative organisms of puerperal sepsis for a long time because most of the investigators used only the aerobic method of culture of the organisms from the uterine swab as well as for blood cultures from septic cases. No wonder that haemolytic streptococci were not obtained in all the septic cases, as the causative organisms may have been anaerobic type of organisms. It was as early as 1910 that Schottmüller in Germany detected these organisms in the puerperal infections but no further notice of it was taken till the second contribution on that subject appeared in 1924 by Dickman who gave records of fatal cases due to that infection. Leonard Colebrook and Hare in 1933, worked out the problem more in detail from bacteriological point of view and discovered four groups of anaerobic streptococci A, B, C & D. These workers have classified the anaerobic streptococci from the colony characteristics.

TABLE 5

TYPE A	Slight buff-colour, produces faetid gas and seen in serious type of infections
TYPE B	Relatively transparent, lack in colour. The gas production is less constant. Seen in the presence of No-infection.
TYPE C	Very black colonies. Less common
TYPE D	Haemolysis on blood agar. Least common

During the investigation of pregnant women I have come across as a routine the type B colonies, and in the few septic cases that were investigated type A colonies were usually seen and type D occasionally. In no case type C colony has been noticed so far.

Schwarz and Brown, in 1936, detected that the development of mild sepsis in the puerperium and thrombophlebitis of the veins of the broad ligament were due to these organisms and the incidence of mild sepsis could be much reduced by instillation of antiseptics.

eg mercurochrome, iodine, and glycerine into the vagina as a routine at the time of delivery

As has been stated before, these organisms are the normal inhabitants of the vagina of pregnant women in 16 to 40 per cent of cases and they require a devitalised tissue for their growth. Hence the lacerated decidual tissue, the blood clots in the uterine cavity and the oedematous lacerations of the cervix are fruitful media for their growth. But during the first 48 hours of the delivery, they are killed by the phagocytes or die from want of suitable acid nutrient medium. At the expiry of 48 hours due to the process of involution of the uterus the tissue exudate in the lochia is progressively acidified by the accumulation of metabolic products and also by the fermentative changes in the lochia themselves. Further, the coincident neutralisation of the antitrypsin of the serum exudate by the tryptic ferments liberated by the disintegration and breakdown of leucocytes affords a better culture medium for the growth of anaerobic streptococci. Colebrook and Hare have found that the serous discharge from the uterus after the 3rd day of the puerperium has a much reduced alkalinity and so much loss of antitryptic power as to facilitate the growth of the anaerobic streptococci.

From pathogenic point of view the anaerobic streptococci have a less invasive action in the healthy tissue so that the lesions produced by them are often of the nature of local sepsis to start with. In the uterus they may behave in two ways. Invading the decidua, they may set up putrid infective endometritis, presenting thick, shreddy, rough surface and leading to offensive discharge. There may be a well formed very thick leucocytic zone which devours the organisms and which raises the effective barrier to them. Thus, very few bacteria are to be seen invading the muscle. If they do, there may develop foci of inflammation and suppuration in the uterine wall, and these on reaching the surface set up localised peritonitis with marked adhesions of the omentum, intestines, the uterus and its appendages, and give rise clinically to a tender mass in the lower abdomen. But if by chance the organisms spread along the thrombosed veins of the uterine wall, they may set up phlebitis of the bigger veins and produce spreading thrombophlebitis of the ovarian veins and the veins of the broad ligaments. Complications like white leg and embolic septic foci in the lungs are quite common. It is rare for the anaerobic infection to produce multiple pyogenic abscesses in the body as the organisms cannot survive long in the normal alkaline blood stream and hence the septicaemia is easily controlled. These are all the present theories as regards the role of anaerobic streptococci in puerperal infection.

Having read these recent publications and the theories in the obstetric literature about the probable role of the anaerobic streptococci it was decided to find out how prominent a role these parasitic organisms play in the infection during the puerperium of those cases in which the other sources eg operative manipulations and perineal tears and lacerations could be excluded. But before the question of

septic cases could be taken in hand, two or three problems came up. They are (1) what is the incidence of the anaerobic streptococci in the vagina of normal patients during pregnancy in this part of the country and among the different social strata of patients (2) whether parity has anything to do with its incidence, (3) if these organisms are present in the vagina, are they likely to give rise to any symptom or a group of symptoms so that clinically they may be useful in suggesting the presence of these organisms in the vaginal discharge. And the last but not the least important consideration is that how many anaerobic streptococcus carriers are likely to develop a mild rise of temperature in the absence of any operative manipulations during the course of labour. But the problem is not solved by these data alone since one should also be able to grow the organisms from the blood-clots from the uterine cavity and the pelvic blood vessels, or from the blood stream. The former is, however, difficult to obtain as there is very little post-mortem material available in these cases since they rarely lead to death unless such complications as general peritonitis, septic embolism pneumonia or lung abscesses develop. The culture of the organisms from the blood is also rather a difficult problem on account of the alkalinity and the high pH value of the blood. Though with good many trials and alterations in the pH of the media used, we could succeed in few of the septic cases we investigated so far. With the present-day advance in aseptic obstetrics, to secure a septic case is becoming rather difficult and furthermore, the type of septic cases that are required for the investigation of this research are still further rare as one wants cases that show septic manifestations without the previous history of any operative manipulations during delivery or any suturing for the trauma in the perineum during childbirth. Such mild fever cases must first be thoroughly investigated with a view to ruling out the question of other febrile conditions during puerperium e.g. malaria, pyelitis, acute cystitis, breast infection, acute flared up tuberculosis in the puerperium. Moreover, as I stated previously the duration of morbidity in the patients may last from three to four days to a few weeks but majority of them belong to the former type and unless the investigator is in contact with the cases right from the beginning and the preliminary necessary investigations, required to rule out the other morbid conditions of the puerperium are carried out without much delay, no really useful material may become available for research work. One cannot at the same time go on taking the vaginal swab soon after labour as a routine in each and every case delivered normally. In such patients the additional factor of exogenous infection is added while taking the swab for preliminary cultural examination and even though these patients may develop morbidity the added factor of exogenous infection cannot be overlooked. Thus one has to wait till the clinical manifestations of sepsis become well developed before the bacteriological investigations of the vaginal discharge are carried out.

In order to avoid the introduction of vaginal speculum to take a swab from the vaginal fornix, in the beginning we collected the material from the vulval pads for the anaerobic culture, from a series of 20 cases as a trial. But there was such a heavy contamination from the anal region because of the rubbing of the pad and the improper cleaning of the anal region after the passage of stools, that a method had to be devised to secure the lochia from the vaginal fornix. The usual vaginal speculi, as they are introduced, carry the organisms from the vulva to the region of the cervix, the lochial discharge there gets contaminated with the skin staphylococci and other skin saprophytes which make the isolation of anaerobic streptococci most difficult. For this purpose a special vaginal speculum was devised and the chances of contamination and also infection by our taking the material, were reduced as far as possible.

Another factor which affects the results of the experiment to a very large extent is the nature of the media used. This will be quite evident as I later on go into the details of the different results secured by making use of varied types of media. I do not wish to bore you with the details of the laboratory methods used as they are not likely to interest you nor do I wish to take up your time in stating the various difficulties we had setting the mechanism in working order.

In short the main theme of the work was to collect the material from the external os and from the region of the posterior fornix of the pregnant patients who had advanced more than seventh month in gravidity. Material was cultured for aerobic and anaerobic growth and at the same time smear was taken for microscopic examination. No attempt was made to study the pH of the vaginal secretion—a most important study necessary for every vaginal smear investigation—as it required a special electric apparatus which was not then available.

Aerobic growth was examined but no further subcultures were made unless a colony of streptococci was obtained. The anaerobic growth was, however, thoroughly investigated by repeated sub-cultures both aerobically and anaerobically so as to decide the absolute and facultative nature of the growth. The final summary of the results obtained so far in the investigations was as follows.

#### THE REPORT OF THE VAGINAL SMEAR

The vaginal flora in the 9th month of pregnancy was investigated in 115 cases. The result of the examinations of the smear of hundred cases out of these was as follows. The last hundred cases were taken so as to facilitate the calculation of percentages.

The Table 6 shows in the last two columns the number of times the same organisms as detected in the vaginal smears could be obtained in the aerobic and anaerobic cultures. The 13 cases, which gave positive vaginal smears for streptococci, had afebrile puerperia which indicates that not all the streptococci present in the vaginal smear are virulent and active.



TABLE 6

Report of the examination of smears of vaginal discharge in 100 cases

List of organisms	Their incidence	Growth of the same organism in culture	
		Aerobic	Anaerobic
Doderlein's bacilli	37%	17	22
Diphtheroids	30%	11	18
Gram—ve Bacilli (including B. coli)	27%	10	7
Streptococci Gram+ve	13%	1	8
No organisms	11%	—	—
No mention of smears	11%	—	—
Gram—ve Bacilli	8%	2	5
Staphylococci	8%	2	5
Yeast	4%	1	1
Gram—ve Cocco-Bacilli	2%	—	—
Gonococcus	1%	—	—
Gram—ve Cocci	1%	—	—
Gram+ve spores	1%	—	—

The result of the aerobic cultural examination from these 100 cases gave the results as tabulated in Table 7

TABLE 7

Aerobic Culture	Total No. of cases studied—100
	Percentage Incidence
(a) Staphylococci	53
(b) Yeast	27
(c) Diphtheroids	26
(d) Doderlein's bacilli	20
(e) Gram+ve bacilli (? Cord)	4
(f) Gram—ve bacilli including B. coli	11
(g) No growth	9
(h) Streptococci	8
(i) Monilla & Filamentous organisms	2
(j) Gram—ve cocci	1
(k) Gram—ve spores	1

It will be seen that aerobic streptococci were present in 8% of the cases. Here I may refer for comparison to the work on cervical culture during pregnancy published in 1941 by Eugene Couti, Macmeans and Lipmann from Pittsburgh Hospital. They found the incidence of streptococci at 14.5 per cent and among these 3.3 per cent were haemolytic. This figure is rather high as compared with my figure which was 8 per cent. Hedley Wright and Taylor in 1930 in their work on haemolytic streptococci had noted these organisms only on few occasions and even these positive aerobic culture cases practically never developed puerperal sepsis. This is because the human pathogenic group A haemolytic streptococcus is present in the vagina, before labour, only on rarest occasion and the organisms which are usually seen belong to B, C and G groups and are hence rarely pathogenic to human being. As I have stated before none of the eight cases with positive aerobic streptococcal growth in my series of 100 cases developed fever during the puerperium.

Those workers who have studied the vaginal flora in different months of pregnancy found a definite decrease in the incidence of positive streptococcal culture after the twentieth week of gestation. In my series as all the cultures were taken in the last month of gestation this fact could not be studied.

#### ANAEROBIC CULTURES

Ninety-eight cases were studied by this method. Out of these, one

series of first 46 cases was cultured on human blood agar slopes and the other series of the remaining 50 cases on the cooked meat medium. For the sake of comparison the results, obtained by both methods, are given together in Table 8.

TABLE 8

Organisms	Anaerobic Culture on human blood agar		On Cooked meat medium	
	Total No	of cases 46	50 cases	Percentage
(a) Staphylococci	28		41	82%
(b) Doderlein's bacilli	18		15	30%
(c) Diphtheroids	13		26	52%
(d) Gram—ve bacilli (? b & c)	7		12	24%
(e) Streptococci	6		27	54%
(f) Gram—ve bacilli with coliform organisms	0		16	32%
(g) No growth	0		—	—
(h) Yeast	5		4	8%
(i) Monilla	1		1	2%
(j) Gram+ve spores	1		1	2%
(k) Gram—ve cocci	1		2	4%

Thus it will be evident that cooked meat medium was found to be the most suitable for the growth of the anaerobic organisms, especially the streptococci and also for their subsequent isolation. It was decided to use the same medium for carrying out the study of morbid cases following normal delivery.

On referring to the figures of the cooked meat medium cultures it is evident that 27 out of 50 cases gave the growth of anaerobic streptococci. The subsequent studies of these strains by repeated subculture, both aerobically and anaerobically gave the information tabulated in Table 9.

TABLE 9

## 27 Cases of Anaerobic Streptococci

2	were obligatory anaerobes
6	were facultative aerobes
19	could not be subcultured on blood agar plates subsequently

Six facultative aerobes showed profuse growth on anaerobic plates but very scanty on aerobic. They have been grouped as facultative aerobes. From the clinical point of view, however, they may be considered as anaerobic and hence only 16 per cent of the patients investigated had strict anaerobic streptococci and none of them subsequently had puerperia.

The figures that I quoted from other workers in the earlier part of this paper are rather high (Elizabeth White 30 per cent, Colebrook 40%, Soule and Brown 39.5%). Whatever may be the cause of this discrepancy in the result, one fact remains that the type of cases that I investigated were comparatively anaerobic streptococci-free patients and further the same fact may account for the absence of morbidity during the puerperia in my series.

Only 12 septic cases were investigated so far. This work was done more for the sake of trial. Eight cases out of them were normally delivered cases while the rest had operative deliveries e.g. forceps, artificial rupture of membranes etc. The results are given here but the number of cases is so small that no definite conclusions can be drawn.

TABLE 10

	Normal labour getting septic (8 cases)			Operative delivery getting septic (4 cases)		
	Smears	Aerobic	Anaerobic	Smears	Aerobic	Anaerobic
Diphtheroids	2	4	4	—	—	—
Gram—ve bacilli	6	3	2	2	2	1
Streptococci	5	2	6	1	1	2
		(Haemo) (one only with Haemo)			(non Haemo) one Non and one Haemo)	
Staphylococci	1	2	1	2	2	2
					(Haemo)	(Haemo)
Doderlein's bacilli	—	1	1			
Monilia	—	—	—			

## NATURE OF OFFENDING ORGANISMS

Normal delivery—8			Operative delivery—4		
1	Anaerobic streptococci with diphtheroids		3	Streptococci growing both aerobically and anaerobically	
2	Anaerobic streptococci				
4	Aerobic haemolytic streptococci with anaerobic staphylo and diphtheroids		5	Haemolytic aerobic and anaerobic staphylococci	
6	Anaerobic streptococci		9	Haemolytic staphylococci.	
7	Haemolytic aerobic and anaerobic streptococci		12	Gram—ve bacilli	
8	Anaerobic streptococci				
10	Pure anaerobic streptococci with diphtheroid and B coli				
11	Gram—ve bacilli				

## NATURE OF ANAEROBIC COLONIES.

8 in Normal delivered cases			Twice in operated cases		
1	Small Translucent colonies B type				
2	Small fine Non Haemolytic colonies A type		One of them was Non haemolytic A D type		
3	Small fine opaque colonies A type				
4	Small fine haemolytic colonies D type				
5	Small translucent and some opaque colonies		A B types.		
6	Small opaque colonies A type.				

## THE RESULTS OF THE SUBCULTURES OF THE GROWTHS FROM COOKED MEAT MEDIUM

In the beginning human blood agar slopes were used for subcultures, but subsequently citrated horse-blood was used. The following table gives the comparison of both the methods and the figures indicate the number of occasions the same growth could be secured in the subcultures

TABLE 11

Subcultures with human blood agar			Citrated horse blood		
Organisms.	C.M.M.	Subcultures	C.M.M.	Organisms	
Staphylococci	12	10	21	20	
Diphtheroids	7	7	17	17	
Streptococci	11	6	11	5	
Doderlein's bacilli	2	1	6	6	
Gram + ve bacilli	4	3	4	3	
" —ve bacilli	1	1	5	2	
Yeast	1	1	3	1	
Sarcina	1	—	1	1	

It will be seen that there is very little difference in the results obtained and hence horse-blood will be used for further research on septic cases

## CLINICAL FINDINGS AND FOLLOW UP OF THE CASES

Among the 50 cases studied with cooked-meat medium, there were 13 primiparas and 37 multiparas. Among them, the occurrence of vaginal discharge was as follows

TABLE 12

	Discharge Present		No discharge	
	8—61%	28—76%	5—38 5%	9—24 %
Primiparas 13				
Multiparas 37				

If only those cases, who had anaerobic streptococci present in the vaginal discharge are taken, they give the following incidence

## ANAEROBIC STREPTOCOCCI GROUP PATIENT—27

	Discharge present		No discharge	
	6—78%	17—60%	2—25%	2—10%
Primiparas 8				
Multiparas 19				

100

100

100

(II) Among multiparas leucorrhoea was much more frequent

(III) The incidence of leucorrhoea is higher both in primiparas and multiparas among those patients who harbour anaerobic streptococci. These patients, however, may suffer from itching.

(IV) Itching was a prominent symptom in patients with yeast, diphtheroids and doderleins bacilli, anaerobic streptococci present in vaginal secretion

(V) Out of 100 cases studied, streptococci could be grown aerobically in only 8 cases. None of them had septic puerperium

(VI) 96 cases were studied for anaerobic growths

(a) Out of them 46 cases were studied on human blood agar and anaerobic streptococcal growth could be obtained in 6 cases only. All of them were obligatory anaerobes—13 per cent

(b) Out of 50 cases studied on cooked meat medium, 27 cases gave +ve growth for anaerobic streptococci—54 per cent. Out of these 27 cases 2 were obligatory anaerobes and 6 were facultative aerobes and 19 could not be grown on subculture on blood agar plate

Thus excluding these last 19 cases, the strict streptococci were present in 8 out of 50 cases. 16 per cent incidence

(VII) Mortality and Morbidity—Among the 100 patients studied no patient had mortality and only 5 cases developed rise of temperature above normal. In none of them, was strict anaerobic streptococcus responsible for the fever as there was history of some sort of operation in three of them

(VIII) Total number of septic cases studied is very small and hence the result of that study is not reported. The main point investigated was the incidence of anaerobic streptococci in the normal vagina of Indian patients and also the best method studied for our work. The cooked meat medium for the isolation of anaerobic organism and citrated horse blood agar for subsequent subculture for determining their obligatory and facultative characters are found suitable and these will be made use of in the investigations of the septic cases later on

#### CONCLUSIONS

Thus a method has been worked out for the study of the vaginal flora and particularly of anaerobic streptococci. The figures are obtained for our Indian patients to indicate the percentage of incidence of these various organisms which may be found in the vagina during the last month of pregnancy, the only symptom they can produce during that time being excessive leucorrhoeal discharge. This work can be used as a basis for the further investigations of the septic cases from anaerobic point of view

(This work was carried out in the Pathology Department of the G. S. Medical College and the earlier part of the work was supported by the grant from the Bombay University in 1941. I have to acknowledge my thanks to Dr. Jivraj N. Mehta, the former Dean of the College, Dr. Khanolkar and Professor Dnyanagade for the full facilities and the guidance offered by them in carrying out this work. I must also extend my thanks to Dr. Wardekar who assisted me in carrying out the bacteriological part of the work and willingly helped me in working on the statistical part of the problem.)

# Society Proceedings

The 36th Scientific Meeting of the Seth G S Medical College and K.E.M Hospital Staff Society was held on Saturday the 8th April, 1944, at 9-15 p.m (new ST) in the Main Lecture Theatre, with Dr R N Cooper in the Chair Dr R V Wardekar read a paper on

## THE 'BLOOD BANK'

This evening I propose to present an account of the blood bank of the K.E.M Hospital My main purpose in reading this paper here, is to invite suggestions as to the measures which should be adopted to reduce the incidence of post-transfusion reactions, especially the pyrogenic I do not intend to go into any theoretical discussions on this subject, but I will attempt to give a general idea about the various procedures that we are following in our blood bank

It was in the beginning of 1942 that we started our blood bank as an emergency measure against the air raids that were expected at that time The scare of the air raids is much less now, but one finds that the blood bank is already an integral part of a general hospital as ours, as can be seen by the following figures of transfusions before and after starting it

In 1940, the average number of transfusions per month was 113% In 1941 the average number of transfusion per month was 124% Since October 1942 the following is the average number of transfusions per month

Number of transfusions given					
Oct. 1942	28	Nov 1942	24	Dec. 1942	50
Jan 1943	37	Feb 1943	43	March 1943	32
April 1943	53	May 1943	55	June 1943	47
July 1943	56	Aug 1943	68	Sept. 1943	60
Oct 1943	52	Nov 1943	49	Dec. 1943	64
Jan. 1944	67	Feb 1944	57		

Recently there has been a move to start a central blood bank for all hospitals in the city, and so it becomes all the more important that we should have one for this hospital and thus lessen the burden on the common bank

The incidence of blood groups among the patients of the K.E.M Hospital based on 1180 blood group determinations is as follows —

AB	I Moss	112	9 5 p c.
A	II Moss.	301	25 5 p c
B	III Moss.	353	29 9 p c
O	IV Moss	414	35 1 p c

## DONORS

A sufficient supply of blood donors has always been a great difficulty Our idea is to use the relatives as donors but many of them whether educated or uneducated are unwilling to donate blood for

one reason or the other. Many of those who are willing to donate blood are anaemic and undernourished. In these hard days when the cost of living has gone so high, many of the donors are semi-starved. Is, then, one justified in bleeding such people even if they are willing to donate blood?

The other group of donors is from the Red Cross Society. It seems that there is a scarcity of donors with the Red Cross Transfusion Society also, as I have often seen the same donor coming over and over again to our hospital. These people donate their blood for monetary reasons rather than from a humanitarian point of view. Naturally, therefore, unless they are well paid there is bound to be a scarcity of such donors. I must say there are some donors with this service, who donate their blood free of charge, every time. Some of the Red Cross donors donate the blood so frequently that they themselves become anaemic and need vigorous treatment. I remember two Red Cross donors who had a haemoglobin percentage as low as 50% and still insisted that they should be bled, as this was one of their important sources of income. Their request was, naturally, not complied with.

Before a donor is bled, malarial infection is excluded by asking for a history of fever and examining the spleen for evidence of enlargement. It is not possible to examine every blood for malarial parasites. As regards syphilis, fortunately from the work of Kolmer on the survival period of spirochaetes in preserved blood, the history of syphilitic infection becomes one of minor importance. He has proved that spirochaetes in the blood preserved at 4—6° C die within about 3 days. Assuming for purposes of discussion that spirochaetes circulate in the blood, there is no danger of transferring this infection to the recipient if it is stored at 4—6° C for a period of 4 days. But such a blood should not be used immediately unless NAB is mixed with it.

#### PRESERVATIVES

Various preservatives have been recommended by different workers. We use I.H.T. fluid or what is known as 'Moscow Fluid', as the preservative. Blood can be preserved in this fluid upto about 25 days without any trace of haemolysis. It is used in equal parts with blood.

The other fluids that are recommended contain sod citrate and glucose in various proportions. Kolmer worked out the comparative values of various preservatives and came to the conclusion that preservatives containing carbohydrate gave better protection to erythrocytes against dehaemoglobinisation, fragility and disintegration and that they were better preservatives for leucocytes and platelets.

It is now known from the work of Bushley that there are three factors which help in preservation of blood: (i) Dilution of plasma by sod citrate (ii) Addition of carbohydrate to the preservative fluid (iii) Vacuum in the bottles.

Oxygenation does not seem to have any effect on preservation.

**MATERIAL REQUIRED**

(1) Fairdeal's bottles were used for collection of blood in the beginning, but as new stock is not available now, we are using another variety of bottle which is of an hour-glass type. The lids of these bottles are not well fitting and so there is always a difficulty in creating sufficient vacuum—the result being that these bottles are not as efficient as Fairdeal's bottles.

(2)  $2\frac{1}{2}$ " or  $1\frac{3}{4}$ " long B.D. needles of size 15, 16 or 17 are used for donors. In females, it is preferable to use size 17.

(3) A transparent rubber tube 10" long.

(4) A specially prepared 6" long needle of the same bore as a 15 size B.D. needle is used for piercing the rubber diaphragm of the lid of Fairdeal's bottles.

(5) A B.D. 18 size needle with a small rubber tube and air filter is used to regulate the vacuum in the bottle.

**METHOD OF STERILISATION**

**Fluids** —The requisite quantity of I.H.T. is filled in clean bottles. The lid is applied loosely and then the bottle is autoclaved at 20 lbs pressure for half an hour. After the autoclave is shut off, the lid of the bottle is screwed tightly while the fluid is still hot. This creates sufficient vacuum in the bottle.

Needles and rubber tubes are sterilised by boiling.

The air filter is sterilised in the hot air oven.

**Collection** Blood is collected by the usual method. Usually there is no difficulty in collecting upto 450 c.c. with this method.

About 5 c.c. of blood is collected at the end, in a sterilised test tube for K.T. or W.R. and a small quantity is placed in sterilised ampoules containing the same preservative fluid. The blood in the ampoule is used for grouping and cross matching, so that the blood bottle need not be disturbed before being supplied.

The blood is tested next day for sterility by means of cultural examination.

**Storage** The blood sample is stored at 40° to 60° C in the cold room. The supernatant plasma is examined every 2-3 days, for evidence of early haemolysis which is seen as a reddish zone of coloration at the junction of the plasma and sedimented corpuscles. If it is present, the plasma is separated by siphonage. It is found that repeated changes of blood samples from cold room to room temperature, bring about an early haemolysis of the blood and because of this it was necessary to make a rule that the blood samples once issued to the ward should not be accepted back in the bank. It is now proposed that the blood samples given to the operation theatre should be carried in specially prepared ice boxes so that even if the blood is not used, it can be sent back to the bank. This will prevent the constant changes in temperature and minimise the chances of haemolysis. Each operation theatre has now been provided with such ice boxes.



Temperature of the blood before transfusion Now it is known that if blood is injected slowly it is not necessary to bring it to the body temperature before transfusion I particularly want to emphasise this fact as two blood samples were spoiled by being kept in boiling water, probably by the nurses or students

*Post-transfusion Reaction* Unfortunately, the maintenance of post-transfusion reaction records has been badly neglected The result is that with the present records it is not possible to give complete statistics of the reactions There is no mention in any of the case notes of any allergic or haemolytic reactions The bloods given in the operation theatre have not been entered in the case notes or in the temperature charts In many cases of pyrogenic reactions also, there is no mention of it in the case notes If this continues it will be impossible to get any instructive data from the transfusions that we give here

Post-transfusion reactions may broadly be divided into three large groups Allergic, Haemolytic, Pyrogenic About the allergic and haemolytic reactions there is no written record, so I will mention only those which I remember

*Allergic* Plasma of Group AB was used in a patient After about 50 c c was introduced, the patient became cyanosed and breathless and complained of constricting pains in the chest The transfusion was immediately stopped—the patient came to normal after about 8 hours It is said that such reactions are seen when the donor's blood is taken after meals Most of our donors come either in the afternoons or in the evenings i e always after meals, and if this be the real cause of the allergic reactions it will not be possible to prevent them in our hospital transfusions as we cannot compel these donors to come in the mornings

*Haemolytic Reactions* Three patients showed haemolytic reaction after stored blood transfusion The common factors responsible for these reactions are faulty matching and the Rh factor In one of these, the Rh factor seems to have been the cause A patient suffering from severe anaemia was given 100 c c of blood After about 7 days, the remaining portion of the same blood was given and this was followed within half an hour by haemoglobinuria In the other two cases the cause could not be found—certainly, it was not due to faulty matching None of these reactions was fatal

*Pyrogenic* Pyrogenic reactions may be classified into three grades Grade I associated with a rise of temperature to 100° F, but no other objective features Grade II associated with a similar or greater rise of temperature and subjectively with feeling of cold and shivering but without an actual rigor

Grade III associated with a definite rigor 1025 blood samples were collected in I.H.T Plasma was separated from 55, i e 5.36% There was haemolysis in 30 samples i e 2.92% and these were discarded

There was contamination in 25 i e 2.43% These were also discarded

So actually the number of samples used for transfusion was 915. There is no record of any reaction in 248 transfusions i.e. in 27.10% and for purposes of discussion these have been omitted and only 667 transfusions are considered. 57 persons expired soon after transfusion—8.56%. There were no reactions in 249 i.e. 37.33%. There were pyrogenic reactions in 361 transfusions i.e. in 54.11%. Grade I, 79 i.e. 11.84%, Grade II, 51, i.e., 7.64%, Grade III, 231 i.e. 34.63%.

As one can see from these figures, the incidence of pyrogenic reaction of grade II is 34.63%. This is very high as compared to 2.2%, the figure quoted by Zimmerman. This high incidence may not necessarily be due to the blood transfusion itself, as it is well-known that reactions depend on other associated conditions.

It is often found that blood transfusions are charged with a certain number of reactions for which they are not really responsible. Most of the patients who are ill and require a transfusion also receive intravenous saline and glucose which may not always be pyrogen-free. It is known that our hospital glucose or saline solution gives rise to pyrogenic reactions after intravenous use. In this series of transfusions, the blood was often mixed with saline or glucose solution and then administered. It is, therefore, very difficult to judge in these cases whether the pyrogenic reactions were due to blood, saline, or glucose.

It has been observed by other workers that pyrogenic reactions are more marked in the following conditions: (i) Blood dyscrasias, leukaemia, purpura, haemolytic anaemia etc. (ii) In febrile rather than in afebrile patients. (iii) Persons suffering from septic diseases. (iv) Patients treated for gynaecological troubles. In our series also, it has been found that gynaecological patients showed pyrogenic reactions in the majority of the cases. In this series all the transfusions were of stored blood and it might be argued that this high incidence of reactions is due to the use of stored blood. This problem has been worked out by De Gown and Hardin and they have come to the following conclusions:

(1) Incidence of all types of reaction was no greater from the transfusion of preserved blood, provided care was taken in storing and handling it.

(2) Variation in the age of the blood caused no corresponding variation in the incidence of reactions.

It can therefore be seen that the reaction statistics are of little value unless they are considered in relation to the indications and the manner of introduction of the blood.

Transfusion can be divided into two parts, (1) collection and storage and (2) actual transfusion. This high incidence of pyrogenic reactions may be due to a defective technique either of collection or transfusion or both.

As has been mentioned at the outset, my main purpose in reading this paper is to try to find out some means to reduce this high incidence of post-transfusion pyrogenic reactions. The important causes of pyrogenic reactions are many. I will take them one by one.

1 Water from which the solutions are prepared The water that we use is obtained by doubly distilling it in a pyrex glass condenser

2 Chemicals used are of a standard chemical company and are recommended for intravenous use

3 Everytime that a new solution is prepared, it is tested for pyrogenic reaction by injecting it intravenously into dogs The normal temperature of dogs is usually between  $100.4^{\circ}$  to  $102.6^{\circ}$  F The temperature of any particular animal is not found to vary over  $1.2^{\circ}$  in the course of 3 hours Accordingly a rise of over  $1.5^{\circ}$  3 hours after injection is taken as definite fever The study of the leucocytic count in dogs shows that the normal range of variation is rather wide but never over 2000 per c mm A drop of 5000 per c mm or over is considered significant With our solutions, the maximum difference in temperature was  $1.0^{\circ}$  and variation in leucocytes was not more than 3000 This test proved that our solutions were pyrogen-free

4 Cleanliness of the apparatus In the early stages of the bank there was a comparatively high incidence of contamination Very careful sterilisation of the skin was not sufficient to prevent it Later on it was found that small blood clots are found in the head of the needle and unless they are regularly removed there are chances of contamination of the blood which is collected the next time We now hardly ever get any contamination of the blood sample

The tube used for collection is of transparent rubber and particles sticking inside can always be seen by holding it against the light Moreover it is very short and so it can be cleaned well

The bottles are hardly removed from the cold room before being issued to the ward and so the chances of haemolysis are minimised

The other factor responsible for pyrogenic reactions is the actual transfusion The method of transfusion in our hospital has not been standardised In some wards it is given mixed with glucose or saline in saline flasks, the top of which is exposed to air except for a thin gauze covering There is no control over the rate of introduction of blood The rubber tubes are very long and one is not sure whether they are cleaned well One of the important causes of pyrogenic reactions is the inadvertent injection of foreign protein matter with the blood, such as may be present in any part of the transfusion apparatus, particularly in the rubber tubing

*Plasma* We are repeatedly asked to supply plasma I have already mentioned the difficulties of persuading people to donate their blood, and unless a sufficient number of people come forward to donate their blood, it will not be possible in this stage of our blood bank to supply plasma Even with these odds we were able to collect 9,800 cc of plasma

To me it appears that it will not be possible to reduce the incidence of these reactions unless a standard apparatus is used for transfusion The main step therefore should be to standardise the apparatus and the technique of transfusion and the thorough cleansing of the appa-

ratus Only apparatus properly cleansed and sterilised by competent technicians in the central preparation room should be used for this purpose

In our series it was repeatedly seen that blood transfusion given in the operation theatre seldom gave rise to pyrogenic reactions One does not know whether it is due to the anaesthesia or due to the clean and well sterilised apparatus of the operation theatre

#### DISCUSSION

**Dr A Hameed** gave his experience on the use of red cell suspension in cases of anaemias The results were encouraging

**Dr V R Khanolkar** speaking about his experience at the Tata Memorial Hospital stressed the importance of proper technique to avoid the reactions Thorough cleansing of the apparatus by a trained team of technicians, strict surgical asepsis, proper matching especially of the groups A and AB and preparation of solutions from freshly distilled water reduced considerably the frequency of reactions The rate of introduction of the fluid should be regularly calculated and in this connection he cited one case in which he was able to demonstrate at the post mortem fragmentation of myocardial fibres due to rapid transfusion He further recommended that regular charts of the intake and output of fluids should be maintained

**Dr K G Munsif** gave an account of 574 transfusions carried out at the Harkisondas Hospital The transfusions were done for anaemias, severe operations, severe infections and haemorrhages Febrile reactions were met with in about 5% In the later cases, improper sterilization of the rubber tubes was found to be the cause In all these, indirect transfusion from the blood of the same group was done and the recipient received pre-transfusion treatment consisting of alkalies and ephedrine—luminal—calcium lactate powders

**Dr R G Ginde** gave his personal experience of 44 cases No haemolytic reactions were met with There was one allergic reaction The frequency of pyrogenic reactions was as follows chills in one case, rise of temperature over  $1^{\circ}$  in six cases and no rise or rise up to  $0.5^{\circ}$  in thirty cases Out of these 13 patients were already having temperature before the transfusion **Dr A V Baliga** remarked that the rarity of allergic reactions attributed by **Dr Munsif** to the pre-transfusion treatment was in his opinion due to improved technique With scrupulous aseptic technique he has succeeded in reducing the frequency of post-transfusion reactions to an insignificant figure He recommended that the patient's relatives, the nursing and the medical staff should be typed and kept ready for an emergency

**Dr S N Kothare** said that the relatives of the Hospital patients are so undernourished and anaemic as to be of no use as donors

**Dr P Raghavan** suggested the use of a questionnaire on the frequency of reactions to be sent with every sample of blood issued from the bank He pleaded for the local treatment of ulcers by red cells for quicker healing

# Critical Notes and Abstracts

## PERNICIOUS MALARIA

Lindsay, D. K. (1948) Guidance notes on pernicious malaria. Trans Roy Soc Trop Med and Hyg 37, 63

Into a highly malarious (100% spleen rate) valley a modern boom brought some 30,000 non-immunes of a dozen races. This mass of susceptible foreigners produced an annual fever rate of 250 per cent and a clinical field of great interest. Col Lindsay remarks 'In a month it was clear that one's 10 years of experience in three continents was worth nothing,' and after three seasons these guidance notes were drawn up for the benefit of newcomers to the district. They are necessarily dogmatic and are meant to apply only to that place, community and period. But to those who see only an occasional pernicious case they reveal malaria as real 'killer'.

*'Pernicious malaria is an acute emergency in which even minutes may count. In no infection other than cholera is death so liable to follow the onset of symptoms so quickly.'*

Four main types are described.

A *Algid* Patient collapses suddenly, cold, pulseless, and often unconscious. Treatment must be immediate with hot bottles, stimulant injections (unspecified) and one pint of intravenous saline containing 6 grains of quinine bi-hydrochloride, (if open operation is needed use a vein on front of ankle).

B *Cerebral* Two distinct varieties

1 *Quiet* Ranges from drowsiness to deep coma, usually with high fever and often incontinence of urine and faeces. Untreated, may live for a week. Treatment by lumbar puncture (relieves pressure and excludes meningococcal infection) and i.v. quinine 6 grains in 10 c.c. 8 hourly until malaria drugs can be retained by mouth. Consciousness does not usually return in less than 18 hours.

2 *Rowdy* Two types, (a) Restless, semi-conscious, noisy breathing, frothing at mouth. (b) Violent, resembling alcoholic intoxication and ranging from chattiness to 'fighting mad'. Must be guarded, and nursed on the floor. Treatment as above and removal of half a pint of blood may be desirable. Mental stability usually restored in 6 to 12 hours. Restless type often fatal.

C *Haemorrhagic* Epistaxis, rectal bleeding, petechial haemorrhages. Generally only one of these features present and often nothing else to suggest malaria. Treatment with i.v. quinine followed by usual drugs by mouth. No success with vitamin K.

D *Gastro-intestinal* Four kinds: persistent vomiting, persistent hiccough, intestinal colic, choleraic (with collapse but rarely urinary suppression). Treatment i.v. quinine until oral drugs retained. Morphine and chloroform sometimes useful in hiccough.

**Blackwater** Usual lines of alkalization and simple diuresis (glucose-bicarbonate drinks, a gallon a day), quinine, atabrin, methylene blue and vitamin K do neither good nor harm. Treat collapse with iv saline and as a general rule leave blood transfusion to convalescence.

The worst kinds of malaria have no resemblance whatever to the popular idea of the disease and the term 'malarial fever' is apt to be misleading. 'The microscope has little place in the diagnosis of pernicious malaria. A negative blood-slide has sent many to the grave' (It would be interesting to know whether thick films stained by Field's quick method were used, and whether death can occur from malaria parasites entirely confined to internal organs and absent from the peripheral circulation.)

Malaria may complicate or be masked by any acute and many a chronic disease. Cerebral symptoms may also be due to co-existing cerebro-spinal meningitis, or in head-injury cases signs of concussion or subdural haemorrhages with blood-stained C.S.F. may be due to malaria. In fact the accident causing the injury may be caused by an attack of cerebral malaria.

In an experience of some 10,000 intravenous injections of quinine the author can recall no untoward effects, though failure to use it promptly has led to many deaths. If necessary it can be given on the roadside. Intramuscular quinine is absorbed more slowly than oral and in pernicious malaria should not be used except for small children. Its popularity as shown by some 2,000 injections given yearly in the bazar would cease were abscesses common and only one such case had been heard of.

Two other points of interest are noted (1) an inversion of temperature below normal may occur for a few days after control of fever at the time when formerly it came on, and (2) the opinion is expressed that sweating and subsequent weakness caused by fluid loss (not blood destruction) can be largely avoided if blankets are withheld.

## QUININE SULPHATE FOR INTRAMUSCULAR INJECTIONS

McGuire and Chakravarty (Ind Med Gaz. 1943 12 610)

Owing to the shortage of quinine bi-hydrochloride, the authors draw attention to the following method of using quinine sulphate for intramuscular injections which they have found to be successful in malaria. About 6,000 injections have been given in the past 12 months without any abscess formation and the therapeutic results have been as satisfactory as with quinine bi-hydrochloride. Even infants, a month old, have been given the injection.

The usual dose for adults is 10 grains, given in the buttocks, though they have used as much as 15 grains in some cases. They found no difference as regards local tenderness after the injection between quinine sulphate and quinine bi-hydrochloride. Their technique of preparation is as follows —

(i) Add 100 minims of dilute hydrochloric acid (B.P.) to 10 c. cm of distilled water and then dissolve 100 grains of quinine sulphate

powder in the above Now add enough distilled water to make the total quantity 20 c cm Each 1 c cm now contains 5 grains of quinine sulphate in solution

(ii) Filter solution through filter paper To prevent the solution being absorbed into the filter paper, first moisten the paper with distilled water

(iii) After filtering, boil the solution and keep in a sterile stoppered bottle It is now ready for use If the solution is not used the same day the required quantity to be boiled again The therapeutic efficacy of the quinine is not affected, in our experience, by double boiling

(iv) Use only dilute hydrochloric acid and not dilute sulphuric acid for dissolving the quinine sulphate, as with the latter the quinine crystallizes to the bottom after a short while

### **DIGITALIS EXTRASYSTOLES**

Sampson et al (*Am Heart Jour*, 26 2 August 1943 177) have shown that the ectopic beats caused by digitalis can be abolished in every instance by the oral administration of potassium salts in doses of 5 to 10 Gm, this is in contrast to the observation of Sampson and Anderson that only 50 per cent of ectopic beats from other causes were affected by potassium salts They present positive evidence that the disturbance of potassium balance in the heart muscle is related to digitalis administration—at least in toxic doses

There was no correlation between the presence or absence of ectopic beats and the fasting blood serum potassium level No significant differences occurred in the curves of the potassium rise and fall in the blood serum in relation to oral potassium acetate doses at any stage before or during digitalis administration—even with toxic doses

When ectopic beats were abolished by the administration of potassium, they failed to return in many instances until long after the blood serum potassium content had fallen to fasting levels This suggests that potassium had become fixed to, or had altered the state of, the cardiac muscle, for the presence of ectopic beats, temporarily at least, was not influenced by the potassium content of the blood serum

### **THE HEART IN ACUTE NEPHRITIS**

Odel and Tinney (*Am Heart Jour* 26 2 August 1943 295) find that cardiac complications are fairly frequent in cases of acute glomerulonephritis, and patients who die during the acute phase may die from heart failure Evidence of obvious cardiac involvement was observed in 16 per cent of 136 cases The cardiac complications varied from murmurs, with or without dilatation, to manifestations of pulmonary congestion or severe cardiac decompensation In cases in which congestive heart failure is a complicating factor, the patient may die suddenly or may improve rapidly, leaving no demonstrable evidence of organic heart disease The hearts of patients who die from cardiac decompensation often show great dilatation, with or without hypertrophy, but dilatation usually dominates the picture Signs of cardiac involvement may appear and disappear rapidly, and

there is no apparent correlation between the severity of the nephritis, the height of the blood pressure, and the incidence or severity of the cardiac complications

## **DUODENAL ULCER SYNDROME CAUSED BY ANKYLOSTOMIASIS**

Venikomshian, H A and Shehadi, W H, *Am Jour Roent and Rad Ther* 49 39 1947

In localities in which ankylostomiasis is common, dyspepsia associated with severe anaemia suggests the diagnosis of hookworm disease, but in countries in which this disease is infrequent ankylostomiasis as a cause of painful dyspepsia is often ignored and not considered in the differential diagnosis. When hookworm disease causes symptoms suggestive of duodenal ulcer a definite diagnosis can be made only by finding the ova of ankylostoma in the stools and by roentgen study of the gastro-intestinal tract. These authors have had patients whose clinical history was suggestive of chronic duodenal ulcer but whose stool contained the ova ankylostoma duodenal and who were relieved completely of their digestive symptoms soon after the infection was cleared up. The fact that some of these patients gave no history of recent haematemesis or melaena and had severe microcytic anaemia prompted the authors to investigate the gastric acidity and to make roentgen studies of the gastrointestinal tract of patients with ankylostomiasis. The estimation of free gastric acidity showed a rise to a higher level than that obtained in duodenal ulcer. In spite of the varying degrees of anaemia, roentgen studies of these cases show evidence of swelling of the duodenal mucosa, inconsistent deformity of the duodenal bulb (duodenitis without an ulcer niche), hyperperistalsis of the stomach and the duodenum and, commonly, reverse peristalsis of the duodenum without obstruction. The administration of a vermifuge resulted in the elimination of epigastric pain within twenty-four hours and the restoration of the duodenal wall to normal within eleven to twenty-four days.

## **GALL-BLADDER DYSPEPSIA**

Moser R H, Rosenak, B D and Hasterlik R J *Am Jour Digest Dis* 9 49 1944

The frequent return of patients because of failure to gain relief from dyspeptic symptoms following cholecystectomy prompted this study. Forty-nine patients having persistent dyspepsia after cholecystectomy for acute or chronic cholecystitis with stones were studied. Control groups consisted of patients who had colic only and were relieved, and those having colic and/or dyspepsia due to the so-called irritable colon.

A comparison of the pre-operative and post-operative symptoms with the histopathology of the gall-bladder showed little or no relationship between the dyspepsia or no relationship between the dyspepsia in gall-bladder disease and the degree of cholecystic pathology.

There were 33 patients whose symptoms were considered to be due to irritable colons, the diagnosis based on irregular bowel habits, cathartic habit, abdominal pain and tenderness, evidence of spasticity



as revealed by the barium enema and relief of symptoms by smooth diet and antispasmodics. It was significant that in 29 of these 33 patients, there were associated abnormalities which probably contributed to the post-operative symptoms. It was concluded that functional colonic disturbances are often responsible for the dyspepsia between attacks of gall-bladder colic and following cholecystectomy.

The next largest group consisted of ten patients with no evidence of disturbed bowel function, who showed improvement promptly on bile-salt medication. It was thought that these were cases of fat indigestion due to a relative deficiency of bile salts in the intestine, probably because of a subclinical reduced hepatic function. Hippuric-acid tests, glucose-tolerance tests, and duodenal drainage were inconclusive.

The remaining patients had well defined entities, including diverticulitis of the colon, superficial gastritis, chronic pancreatitis, biliary dyskinesia, and one had chronic pelvic inflammatory disease.

From the study the writers concluded that no definite entity of gall-bladder dyspepsia could be established, and that the food intolerance in gall-bladder disease is identical with that encountered in a variety of gastro-intestinal disorders. When dyspepsia was associated with colic, relief followed cholecystectomy; however, interval dyspepsia was not thus relieved and should not in itself be considered an indication for operation.

# The Indian Physician

VOL III NO 7

JULY 1944

WHOLE NO 31

## Original Contributions

### PHRENIC EVULSION IN THE TREATMENT OF PULMONARY TUBERCULOSIS

A REPORT OF 109 CASES

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Failing the discovery of any specific chemotherapeutic agent in the treatment of Pulmonary Tuberculosis, the tuberculosis worker has to depend on the time honoured line of "Rest" treatment. General rest is, however, not enough and of late years many new methods have been employed to provide local rest to the affected lung. Adequate rest of the diseased lung by the so called "Collapse Therapy" in the treatment of pulmonary tuberculosis has now established itself as a recognised advanced measure of paramount importance during the past four to five decades in our fight against this human scourge and today we see thousands of tuberculous patients, thus managed, practically returned to normal life.

In pulmonary tuberculosis, like tuberculosis elsewhere in the body, in addition to the local destructive lesion of the tissues as a result of the activity of Koch's bacillus, a continuous flow of toxins (frequently accelerated by the mobility of the tissues involved) proceeds at all times into the circulation producing tuberculo-toxaemia which is responsible for the severe constitutional symptoms of the disease such as fever, malaise, loss of weight, sleeplessness, increasing general debility and the downhill trend of the patient's resistance to the invading organism.

With the progress of the disease this increasing toxaemia further inhibits the defensive mechanism of the individual and so the vicious circle once started continues, till the sad chapter of the patient's life

is closed. Luckily, however, it is possible to control the absorption of toxins by the various current methods of Collapse Therapy, the rapid reduction of the toxæmia which follows the successful collapse of the lung is mainly the result of interference with pulmonary circulation and lymphatic drainage.

The best and the safest method of bringing about ideal collapse of the lung is artificial pneumothorax, but its use, unfortunately, is limited to less than half the cases, because of pleuritic adhesions permitting either no introduction of air at all or at the most an inappropriate collapse. No doubt Intrapleural Pneumolysis renders successful artificial pneumothorax possible in some cases, there still remains a large group of cases where the adhesions do not lend themselves with safety to this operation either as a result of their multiplicity, extent or their unsuitable locations. Thus in our series of 109 cases artificial pneumothorax failed altogether in 41 cases and further in 39 cases it had to be abandoned after some period. Ukil (1937) states that barely 10 per cent of the cases are found to be suitable for artificial pneumothorax therapy. In such cases it is better to resort to other methods of bringing about the collapse of the diseased lung like phrenicectomy, extrapleural pneumothorax and thoracoplasty rather than to persist with an ineffective and perhaps useless pneumothorax over prolonged periods in the vain hope that the pulmonary lesion would heal.

According to some observers a period of 6 months is enough for the complete healing of the pulmonary lesions and on this basis the operation of phrenic interruption was evolved but in actual practice this fortunate state of affairs does not mostly prevail in this country and the treatment has to be prolonged beyond the limits imposed by a temporary interruption of the nerve supply of the diaphragm and further in a fairly large number of these cases this partial collapse has got to be supplemented by thoracoplasty. It would, therefore, appear that one could play for safety if the interruption of the nerve is complete and permanent which would not only offer the diseased area longer rest but should circumstances demand a major operation later on prove a very sound preliminary measure.

The operation of Phrenic evulsion consists in exposing the nerve in the neck and after its division evulsing it, an operative procedure by which the intrathoracic part of the nerve is pulled out.

#### ANATOMY

The Phrenic nerve, the nerve supply of the chief muscle of respiration—diaphragm, arises in the neck chiefly from the 4th cervical and in addition it receives a branch from the 3rd and another from the 5th. Very rarely it receives additional fibres from the 6th, 7th and 8th. The 3rd and 4th join at the lateral border of the scalenus anterior to form a trunk which crosses the anterior surface of the scalenus anterior from the lateral to the medial side behind the prevertebral fascia which lies in front of the scalenus anterior and descends to the root of the neck beneath the sternomastoid. Inferior belly of the omohyoid, transverse cervical and transverse scapular vessels. The nerve next passes in front of the sub-clavian artery separated by the scalenus anterior muscle behind the corresponding vein and enters the thorax behind the sternoclavicular joint. In the thorax it descends vertically in front of the root of the lung to the diaphragm accompanied by the pericardiaco phrenic branch of the internal mammary artery and divides into branches which pierce that muscle. One or some times two small phrenic roots arise from the 5th, pass downwards and join the main phrenic trunk. The relations of the phrenic nerve in the region of the superior mediastinum vary on the two sides. On the right side after being crossed by the subclavian vein the nerve descends vertically in close association with right innominate vein and the superior vena cava. On the left side the nerve runs between the left common carotid and the left subclavian artery where it is crossed by the vagus nerve.

The twig from the 5th cervical may arise from the Brachial Plexus from the nerve to the subclavius or jointly with the suprascapular nerve and join the main nerve some where between the 1st rib and the hilum of the lung. These accessory phrenic nerve fibres may take different courses some of which are shown in the accompanying diagram (Diagram I see Plate). Statistics show that there are generally abnormalities present in between 20-30 % cases. Simple division of the nerve in the neck will not therefore completely paralyse the diaphragm on the operated side as these fibres from the 5th would not be affected in such cases. The object of evulsion is to pull the nerve out of the diaphragm and thus not only remove the main nerve but also the accessory phrenics.

## PHYSIOLOGY

The Phrenic nerve in addition to containing motor fibres supplying the diaphragm contains sensory and sympathetic fibres. The sensory supply of the peripheral part of the diaphragm is referred to the anterior abdominal wall. The central part of the diaphragm receives its sensory supply from the phrenic nerve and sympathetic fibres contained in it. Stimulation of this portion of the diaphragm causes pain which is referred to the supra-clavicular region and shoulder joint through the cervical plexus. The pull on the phrenic nerve during evulsion in almost all cases produce a sensation of pull at the diaphragm and the heart region probably through sympathetic nerves in the region of the heart and diaphragm both of which are lifted during traction upon the nerve. During inspiration the diaphragm contracts and the dome descends, where as during expiration the muscle relaxes and the dome ascends due to the positive intra abdominal pressure. This descent of the diaphragm allows expansion of the lung affecting mainly its lower and posterior portions.

## EFFECTS OF PHRENIC EVULSION

1 Complete paralysis of the diaphragm on the operated side (cessation of active movements), the muscle fibres gradually atrophy and fibrose, the paralysed hemidiaphragm assumes expiratory position as a result of positive intra-abdominal pressure.

2 If seen under a fluoroscope, the paralysed half of the diaphragm is motionless on quiet breathing, but on deep breathing it shows paradoxical movements i.e. ascends during inspiration and descends during expiration.

3 The diaphragm ascends from  $\frac{1}{2}$ " to 4". The height to which the diaphragm will rise after the operation in any particular case cannot be foretold with exactitude. In certain cases there is no immediate rise but after the lapse of several weeks there is a marked rise of the diaphragm. However, this marked upward ascent of the diaphragm may be prevented in spite of complete paralysis by the presence of pleural adhesions in the lower zone or due to thickened basal pleura. As a result of loss of the normal diaphragmatic contractions, expansion of the lung is incomplete. The volume of the lung on the operated side is reduced from  $\frac{1}{6}$  —  $\frac{1}{3}$  of its total volume as a result of the decreased volume of the hemithorax. The collapse may affect the diseased lung tissue, normal lung tissue or both. In the absence of adhesions the collapse is mainly selective.

4 The condition of the underlying lung also influences the rise of the diaphragm to some extent thus when the lesion is of the exudative type with the alveoli filled with exudate the lung is not easily collapsible and consequently the rise of the diaphragm is the least but where the disease is of chronic productive and proliferative type with extensive fibrous changes, the rise is the greatest.

5 The partial collapse is not limited to the base of the lung as cavities near the apex are often greatly reduced in size. The ultimate result of the operation is partial rest to the affected lung.

*Preparation* —If a pneumothorax is present in the ipsilateral side, some air should be aspirated or the operation performed shortly before a refill is due in order to avoid sudden post-operative dyspnoea resulting from an undue increase in the intrapleural pressure from the elevation of the diaphragm. The patient is encouraged to expectorate

the sputum particularly shortly before operation Half an hour before the operation the patient is given hypodermic injections of morphia 1/6th gr with atropine 1/100 gr

#### OPERATION

*Position of the patient on the operation table*—The patient is made to lie on the back with a flat pillow under the shoulder blades and the face is turned to the opposite side

*Anaesthesia*—Operation is performed under local anaesthesia using ½ per cent novocain solution A dermal wheal is raised with a fine needle at a point just in front of the posterior border of the sternomastoid about a finger's breadth above the clavicle Through this wheal about 4-6 c c of ½ per cent novocain is injected interdermally and subcutaneously for 2½" along the line of the proposed incision or a little beyond that A few c c of novocain is injected along the middle of the posterior border of the sternomastoid There is no necessity of infiltrating the deeper tissues (A case of aneurysm of sub-clavian artery is reported (Alexander) which resulted from a surgeon having passed an anaesthetising needle deeply and blindly into the base of neck)

*Technique*—The nerve is exposed through 1" to 1½" long transverse incision in the skin crease a finger's breadth above the level of the clavicle extending from the posterior border of the sternomastoid outwards The skin, subcutaneous tissue, platysma and the deep cervical fascia are divided Rarely the external jugular vein may have to be divided between artery forceps and ligatured but we have found this seldom necessary The posterior border of the sternomastoid is retracted well forward The fibrofatty tissue beneath the investing layer of the deep cervical fascia and in front of the prevertebral fascia is separated by inserting Mayo's scissors and carefully opening it The omohyoid muscle which is frequently exposed under the fascia is retracted upwards The scalenus anterior is recognised and the transverse cervical vessels are seen crossing the muscle transversely Care should be taken to avoid injuring these vessels The brachial plexus is the best land mark for the recognition of the scalenus anterior It lies between the scalenus anterior and the medius The phrenic nerve is usually readily recognised as it crosses the scalenus anterior muscle behind the anterior sheath (prevertebral layer of the deep cervical fascia) from the lateral to the medial side At the root of the neck the nerve is seen on the medial aspect of the muscle and will be seen only when the sternomastoid is retracted well forward In some cases where the patient has enlarged lymph glands it is necessary to incise the sheath before one can see the nerve At times it is difficult to find the nerve because it is retracted along with the fascia Having exposed the nerve, a few drops of novocain ½ per cent solution are injected into the nerve The fact that it is the phrenic nerve can positively be settled by stimulating it below the point of injection when contraction of diaphragm will occur The nerve is divided and distal end is grasped by an artery forceps It is then gradually pulled

out by winding it over the forceps. Special forceps are used by some surgeons but an ordinary Spencer Wells artery forceps serves the purpose. Usually the whole of the nerve comes out of its insertion from the diaphragm but in a few (amongst our series in 3 cases only) the nerve gave way and only 2-3 inches of it were pulled out. The retractors are withdrawn, the platysma is sutured with catgut and the skin with fine silkworm.

*Difficulties* —These are mainly encountered because the nerve is not found in its normal position and much time is spent in locating it. It is in such cases that the vagus or the sympathetic run the risk, of being cut instead of the phrenic. The most satisfactory means of differentiating the three nerves that lie anterior to the scalenus anterior is to trace the unidentified nerve upwards, if it springs from the cervical roots of the brachial plexus, it is neither vagus nor sympathetic but almost surely the phrenic. Stimulation of the nerve by pinching it causes a sudden contraction of diaphragm which can be felt by a hand placed upon the epigastrium and the patient complains of pain in the shoulder region.

Care should be taken that the pre-vertebral layer of cervical fascia that covers the scalenus anterior is not violated, as the nerve is frequently retracted out of the field before it is seen.

We have not failed to find the main phrenic nerve so far though in a few cases it has taken an hour or so to find it out. If it is not found in its usual position it should be sought for at the medial edge of the scalenus anterior.

In some cases the nerve is densely adherent to the mediastinum (especially where mediastinal pleurisy has existed) and evulsion is not possible. The nerve breaks after only an inch or so has been pulled out. The distal end retracts into the thoracic cavity. In such cases in order completely to paralyse the hemi-diaphragm, all communicating fibres between the phrenic and the cervical nerves are cut.

*Complications* —A large number of serious complications such as damage to the blood vessels, tearing of the sub-clavian vein, air embolism, haemoptysis, damage to the sympathetic or the vagus nerves and lastly various psychic and reflex disturbances have been reported but in our series of cases we have not come across any of the serious complications. A post-operative rise of temperature lasting for a few hours occurred in some of our cases while in one female case there was vomiting which lasted for two days.

*Indications* —

1 As an independent procedure

(a) In cases where artificial pneumothorax has failed because of adhesions and the intrapleural pneumolysis is not feasible.

(b) In basal lesions. It is of great value in cases with basal lesions as it produces selective collapse.

(c) *Haemoptysis* —

In those cases of haemoptysis where artificial pneumothorax is impossible while thoracoplasty is contra-indicated.

(d) *For social and economic reasons —*

In cases where the financial resources of the patients (particularly in India) do not permit a lengthy course of pneumothorax therapy, the feasibility of phrenic evulsion should be seriously considered

2 *As a preparatory operation to thoracoplasty* for the following reasons —

(a) As it is impossible to predict the course of the disease, the preliminary phrenic evulsion may in certain cases suffice to bring about clinical cure and thus save the patient from the risks of thoracoplasty while in others it may improve the condition of patient so much as to make the patient stand the thoracoplasty operation better

(b) Due to its beneficial effect on cough, the possibility of aspiration infection is reduced (Ralph C Matson & Ray W Matson 1939)

(c) As it reduces the cavity of hemi-thorax due to the rise of the diaphragm the number of ribs to be removed later on are correspondingly reduced

(d) Last but not the least the object of operation in some cases is to test the ability of the contralateral lung to stand the major operation, but its value in this connection is doubted by some (Head 1934)

3 As an adjunct to artificial pneumothorax on the same side where there are adhesions preventing an affective collapse to provide an additional collapse

4 Before stopping artificial pneumothorax, specially when the extent of the involvement of the lung has been known to be extensive before the institution of artificial pneumothorax (Benjamin 1935) -The idea is to reduce the cavity of hemithorax into which the lung has to expand in order on one hand to avoid strain on the fibrosed areas produced as a result of healing and on the other to lessen the chance of possible retraction of the mediastinum and its contents

5 *On Bilateral Cases —*

Artificial pneumothorax is instituted on one side while the phrenic evulsion for the affection of the opposite side

*Contraindications —*

1 Very low cardiac reserve especially when the respiratory functional reserve is also low

2 Extensive bilateral disease

*A brief analysis of the cases —*

Total number of cases done was 109 As a sole surgical procedure i.e primary phrenic evulsion was performed in 54 cases and as an adjunct to artificial pneumothorax or thoracoplasty i.e secondary phrenic evulsion was done in 55 cases Out of these, 61 were male and 48 female cases

*Rise of the Diaphragm —*

In our series the extent of the average rise of the diaphragm was 1" and 1 1/3" In a few cases (3 to 4) there was practically no rise while in others it had risen as high as 3rd rib (From our experience we find that the ascent of the diaphragm is further reinforced by the use of pneumoperitoneum) In three of our cases, the length of the

nerve remove was only 3" while in others practically the whole length of the nerve was removed

It should be noted that the rise of the diaphragm did not occur immediately after the operation. It required several weeks to months to reach the maximum limit

#### Classification according to the stage of the disease

Stage	Stages of the disease —		
	A	B	C
I	1	nil	nil
II	2	6	11
III	6	14	60

(N.B.—The classification followed is according to the report of the Sub-Committee on Classification of Pulmonary Tuberculosis, published by the Tuberculosis Association of India, July 1940, New Delhi)

Out of the total number of cases single or multiple cavities were found in 43 cases. They were distributed as follows —

Upper zone 25 Middle zone 14, Lower zone 4

#### Results of the operation —

1 *On the Tubercle Bacilli* —In our series of 109 cases, 96 i.e., 88 per cent were sputum positive cases before the operation. 10 i.e., 9 per cent were negative while 3 cases had no sputum at all. After the operation, 34, i.e. 31 per cent out of these 96 positive cases became negative for acid fast bacilli while 10 cases who were negative before the operation remained so all through.

2 *On Cavities* —As already pointed out the cavities were located in altogether 43 cases and their localization and the results are as follows —

Localisation	No. of cases	No. showing complete disappearance	No. showing shrinkage	Negative results
Upper zone	25	2 8%	11 44%	12 48%
Middle zone	14	4 28.5%	8 57%	2 14.5%
Lower zone	4	3 75%	1 25%	

3 *On Symptoms* —Due to the relaxation afforded to the lung the troublesome cough is greatly relieved and expectoration facilitated. In the beginning the expectoration may be increased in amount due to the establishment of proper drainage and clearance of the stagnant material of the diseased area but after a few days it is also diminished along with the clinical improvement of the case. Owing to the diminution or obliteration of the cavities and of the lymph and venous stasis there is diminished absorption of tubercle toxin and a consequent reduction of pyrexia and improvement in general health. The sedimentation rate of blood is also correspondingly lessened.



## RESULTS IN RELATION TO THE STAGE OF THE DISEASE

Stage of the disease. Arrested	Much improved	Improved	Satittonery	Worse	Died	Total
IA	1					1
IB						
IC						
IIA	2					2
IIB	2	4				6
IIC	3	5	2	1		11
IIIA	2	3	1			6
IIIB	2	7	4	1		14
IIIC	2	13	50	2	2	69
Total	1	13	82	57	4	109

Two deaths shown above, did not occur as a result of the operation but the patients died after a year due to extension of disease

## A few case reports to illustrate the result of treatment

**Case 1** K. C. 39 years complained of fever cough with expectoration and increasing debility. Duration 6 months. Temperature averaged 101.5°F, pulse 120, S. R. 106 m.m. weight 140 lbs., sputum positive urine contained sugar Lungs—diminished breathing with fine crepitations on the right base and a few occasional crepitations on the left base Skiagram—dense exudative lesion on the right base while fine mottling on the left base. (Fig IA) Treatment—General, Insuline therapy and phrenic evulsion on the right side. Remained under care for 8 months, became afebrile after two months of the operation and at the end of the treatment S. R. 15 m.m. pulse 85, sputum negative, gained weight by 12 lbs. Skiagram taken 3 months after the operation showed a rise of the diaphragm by 2½" and a marked clearing up of the lesions especially on the right side. (Fig IB)

**Case 2** R. B. 20 years, complained of fever cough with expectoration and pain on the right side. Duration one year. Temperature range 98.8°F—102.4°F pulse 125, marked emaciation, sputum positive, S. R. 110 m.m. weight 85 lbs. Lung—bronchial breathing in the right infracavicular region with coarse crepitations all over Skiagram—dense patchy opacities on the right side with two cavities—one below the clavicle and the other in the lower zone, left side clear (Fig IIA.) Treatment—General, artificial pneumothorax and phrenic evulsion on the right side. Remained under care for 9 months. Artificial pneumothorax unsuccessful and phrenic evulsion performed on the right side. Temperature gradually came down to normal. At the time of discharge, ambulatory S. R. 18 m.m. weight gained by 20 lbs, sputum negative, and the skiagram showed rise of diaphragm by 3" and closure of both the cavities (Fig IIB)

**Case 3** R. K. 36 years, complained of fever cough with expectoration and occasional attacks of pain on the right side. Duration 4 months. Examination—Temperature averaged 101.6°F, pulse 115, S. R. 98 m.m. marked emaciation, weight 74 lbs. sputum positive Lungs—a few crepitations right upper zone and diminished breathing in the right lower zone. X ray—patchy infiltration right upper zone with a small cavity in the middle zone and a small amount of fluid on the same side (Fig IIIA) Treatment—General artificial pneumothorax and right phrenic evulsion. Remained under care for three months. Artificial pneumothorax unsuccessful due to adhesions. Right phrenic evulsion was done. Temperature came down to normal S. R. 37 m.m. gained weight by 25 lbs, sputum remained positive. X ray—rise of diaphragm by 3½" but still there was a little fluid in the pleural cavity (Fig IIB) Advised thoracoplasty but refused.

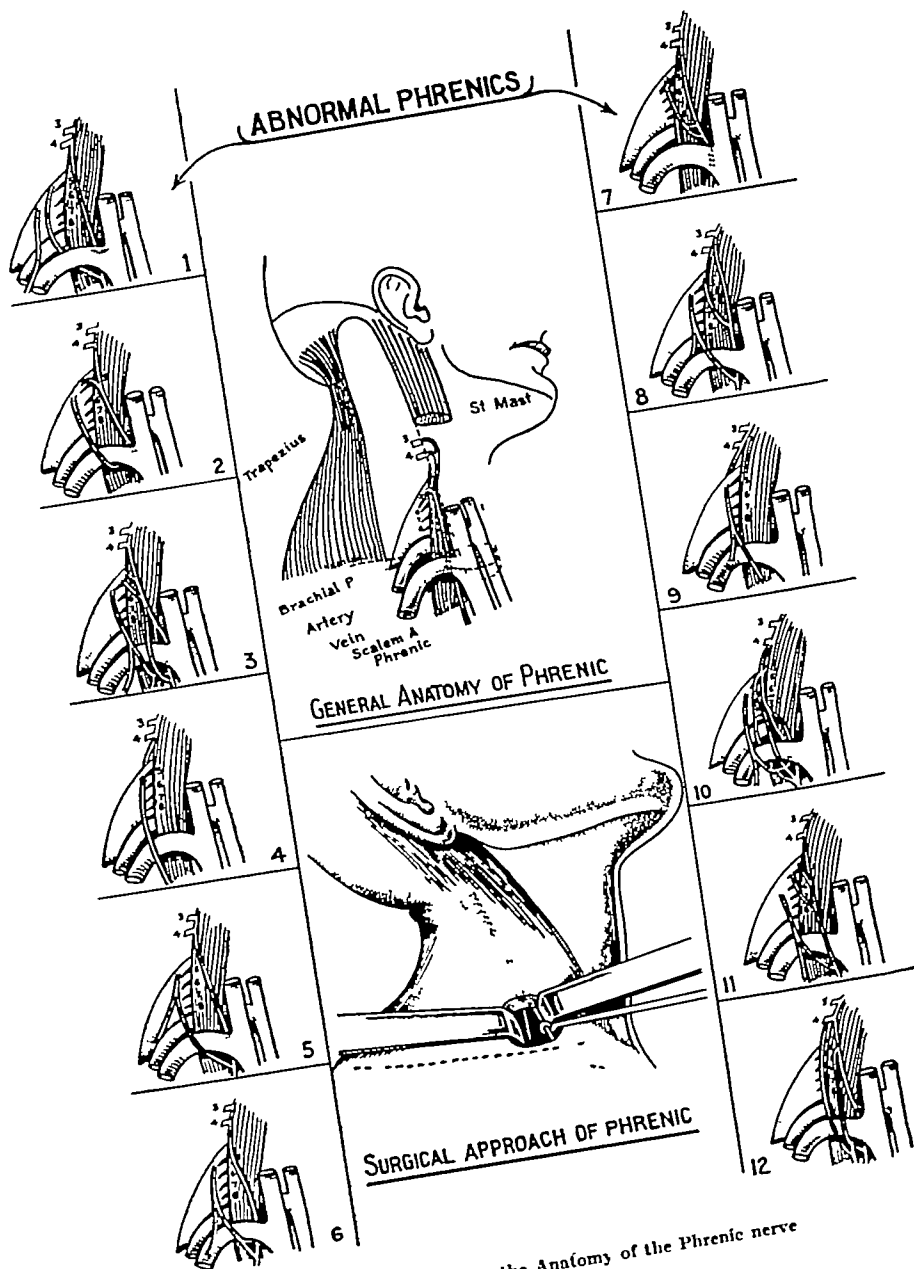
**Case 4** Z. A. 25 years, complained of fever and cough with expectoration. Duration 8 months. Examination—Temperature averaged 100.0°F, pulse 110 S. R. 85 m.m., Sputum positive Weight 96 lbs. Lungs bronchial breathing with coarse crepitations right lower zone and a few fine crepitations left upper zone Skiagram—A cavity and tubercular infiltration in the upper part of the right lower zone and small patchy infiltration (left infracavicular region (Fig IVA) Treatment—General Artificial pneumothorax, right phrenic evulsion. Remained under care for 7 months Right artificial pneumothorax failed and phrenic evulsion was done After 1 month became afebrile. S. R. 8 m.m. Sputum: negative, cough disappeared, gained weight by 18 lbs Skiagram—rise of diaphragm by 3½" closure of the cavity and marked clearance of the lesions (Fig IVB) He was working in the garden attached to the Sanatorium for 3 hours daily without any untoward symptoms

**Conclusions**—109 cases of Pulmonary Tuberculosis mostly i.e. 81 per cent in stage III treated by Phrenic evulsion are reported. From the marked beneficial effects of this procedure in 42 per cent of our cases, without any operative mortality or post-operative complications,

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Fig. 1 A Before Operation Tubercular Fig. 1 B After Operation Tubercular Fig. 2 A Before Operation Tubercular Fig. 2 B After Operation Tubercular Fig. 3 A Before Operation Tubercular Fig. 3 B After Operation Tubercular Fig. 4 A Before Operation Tubercular Fig. 4 B After Operation Tubercular



Figures illustrating the Anatomy of the Phrenic nerve

and the disappearance of T B from sputum in 31 per cent of our cases (a fact of great Public Health importance) it should appear that Phrenic evulsion is a measure of supreme importance in suitably selected cases of Pulmonary Tuberculosis

2 Since Phrenic evulsion produces limited pulmonary relaxation as compared to a successful Pneumothorax or complete Thoracoplasty, the results cannot be expected to be fully satisfactory in patients with extensive old lesions and advanced excavations

3 The importance of this operation as a preliminary to thoracoplasty has been amply stressed

4 Lastly, for economic and social reasons, particularly in this country where proper institution management and control of pneumothorax is difficult, it would perhaps be more useful to consider the institution of phrenic paralysis in suitable early pulmonary basal lesions rather than to embark upon artificial pneumothorax with all its attendant risks of sepsis, trauma, pleuritis and the not uncommon difficulty of its supervision and maintenance, further handicapped by illiteracy and superstitious mentality of an average Indian patient of lower classes

We would like to thank Drs R. C. Khanna, S K. Gupta, Gurinderjit Kaur and particularly Dr Chaman Lal for their help in the compilation of the results and general assistance in the preparation of this report. We are also indebted to Professor M. A. H. Siddique for the diagrams of the Phrenic Nerve. We are also grateful to Colonel R. Hay, C. I E., I.M.S. Inspector General of Civil Hospitals, Punjab, for his keen interest in the Anti tuberculosis Unit at Amritsar

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*Continued from p 254 .*

#### TREATMENT

The treatment of the condition has changed somewhat recently, more stress being laid on a high protein as well as on a high carbohydrate content in the diet. As a result of experimental work in certain types of poisoning, such as that of Miller, Ross & Whipple (1940), with chloroform in dogs, it has been considered that proteins with high content of the sulphur-containing amino-acids, methionine, and cystine, might be of value in the treatment of this condition (B.M.B Vol I 1943 10 112)

# Society Proceedings

The 37th Scientific Meeting of the Seth G S Medical College Staff Society was held on Saturday the 10th May 1944 in the Main Lecture Theatre of the College Dr V R Khanolkar was in the chair Dr R N Cooper read a paper on

## TUMOURS OF THE TESTICLE

Our views about the pathology and treatment of malignant tumours of the testis are not sufficiently standardised This has prompted me to bring this subject before you I do not wish to bore you with an exhaustive paper on this subject but I wish to limit myself to a few salient features as indicated in the synopsis already circulated

Through the courtesy of Professor R G Dhayagude, I am able to give you an account of 29 cases of malignant neoplasms of the testis as recorded at the Pathological Department of our college between the years 1930 and 1943 To this I have to add three cases from my private practice From these cases certain interesting conclusions can be drawn

### Age Incidence —

- 3 cases between 1—3 years
- 1 case at the age of 15 years
- 10 cases between 20 to 40 years
- 3 cases between 41 to 50 years

In three cases the age is not recorded Classified by the Department of Pathology, there were

- 14 Seminomas
- 5 Embryonal carcinomas
- 7 Carcinomas
- 2 Adenocarcinomas
- 1 Interstitial cell tumour

The duration varied from 4 months to 3 years There were 6 cases with enlargement of the regional nodes 5 cases probably started in retained testes, and 2 cases gave a history of "strangulated hernia"

There is a great deal of controversy with regard to the classification of tumours Where giants differ, it is not unwise to suggest a classification which appears to be fairly practical

As tumours eventually develop from an altered proliferation of a cell, it is important to observe that the testicle contains three types of epithelial cells, the Germinal cell, the Sertoli or Basal cell also called the trophocyte, and the Leydig or Interstitial cell In addition there are possibilities of growth from (a) Lymphocytic cells (b) Muscle cells, and (c) Suprarenal rests

The following is the classification suggested

- |                   |  |
|-------------------|--|
| (A) Homologous    | Sarcomas   |
|                   | Monocellular Seminomas   |
| (B) Heterologous  | Adult teratomas (Least malignant)  |
|                   | Embryonal tumours derived from totipotent sex cells which may show preponderance of— |
|                   | 1 Trophoblastic elements (chorion—epithelioma)                                       |
|                   | 2 Hypoblastic elements (Embryonal adenocarcinoma)                                    |
|                   | 3 Mesoblastic elements (Mixed Sarcoma)   |
|                   | 4 Epiblastic elements (Neuro-epithelioma)  |
| (C) Miscellaneous | Interstitial cell tumour   |
|                   | Suprarenal rests   |
|                   | Hodgkin's disease.   |

Adult teratomas are the least malignant and form 10 per cent of the total bulk. They consist of tumours containing a mixture of adult tissue, similar to those found in the mediastinum and elsewhere. They are believed to be derived from adult blastomeres. They have no relation to the embryonal group. Gonadotropic hormone is not found in the urine. These tumours are potentially malignant. When malignancy does occur it does so during the so-called cancer-age (i.e. after 40). They metastasize rarely and late. Our series does not contain adult teratomas, and also we do not possess a specimen of chorion-epithelioma, however, Dr Khwaja of the J J Hospital, some time ago demonstrated a case of extensive metastasis with a small nodule of chorion-epithelioma in the testis.

We have only one interstitial cell tumour. All the others are either seminomas or embryonal teratomas.

The detection of hormones in the urine of patients suffering from neoplasms of the testis has led to a great deal of progress in the scientific study of these neoplasms.

In 1921, Zondek first observed the appearance of a gonadotropic hormone in the urine of a man suffering from teratoma testis, and 3 years later reported his observations in respect of 14 cases of teratomas.

In 1931, Ferguson observed that irradiation of the tumour caused the disappearance of the hormone from the urine. He also demonstrated the methods of quantitative estimation of Prolan A excreted in the urine and showed that the amount of hormone excreted varied with the type of tumour present. The amount of hormone increases in proportion to the embryonal characters of the neoplasm. Chorion-epithelioma causes an excretion of Prolan A in urine in excess of 50,000 mouse units per litre. Embryonal adenocarcinoma 10,000—40,000 units, teratoma of adult type 50—500 units, sarcomas and seminomas—no hormone. Amounts over 50 mouse units per litre alone, justify a diagnosis of malignancy. In one case of an elderly gentleman, there was a history of recent painful enlargement of the right testis. Clinical diagnosis lay between tubercle and malignancy. A hormonal test was done and was found to be positive. A quantitative estimation was not done. Orchidectomy was performed with the tentative diagnosis of malignancy. The testis was sent to the same pathologist and the diagnosis was given as tuberculosis.

This test is further helpful in judging the radio-sensitivity of tumours. Should hormone disappear rapidly after irradiation of the primary tumour, it may be deduced that the tumour is radio-sensitive. The reappearance of the hormone in a case treated either by operation or irradiation indicates that recurrence has occurred. In fact the urine test is positive from 1-3 months before metastatic lesions or local recurrence can be detected clinically.

From the clinical standpoint, cases may be divided into those where the patient comes for a testicular swelling or those where the patient seeks help for the metastases, as the primary growth is insignificant.

If the patient comes for a testicular swelling, it is found that the swelling is painless. There is a sense of weight. The golden rule is that

any painless swelling of the testis should arouse the suspicion of malignancy. Palpation shows that the normal shape of the testis is preserved. In the early stages, the surface of tumour is smooth. Later nodules and irregularities occur. In the early stages, the epididymis may be felt as a nodular cord but later it becomes lost in the enlargement. Hence in the early stages, it is possible to mistake the tumour for a tuberculous affection.

The probable mistakes in diagnosis are — (1) Hydrocele, (2) Haematocele, (3) Pyocele, (4) Tubercle, and (5) Gumma.

The other type of case is where either the primary growth is insignificant or the metastatic deposits overshadow the picture and the apparent testicular swelling is not attended to. Thus in a case of a Parsi youth aged 22, there was a fever with rigors and a swelling was palpable in the splenic area. It was variously diagnosed as splenic or a kidney mass. Intravenous pyelography showed a normal right kidney. The left kidney did not show up. Naturally the diagnosis of hydronephrosis was maintained. An important surgical aphorism is that in every case of testicular swelling, palpate the abdomen for paraortic lymph nodes and in every case of an abdominal lump examine the testis for a possible growth. Relying on this I examined the testis and found a painless swelling of the left testis. The patient stated that he had been hit with a cricket ball 5 or 6 years ago, and that his condition had been diagnosed as a haematocele. I suggested a hormonal test. This was not done. The fever came down, the lump seemed to be smaller. A series of X-ray pictures was taken. The left kidney would not show up. The swelling in the abdomen completely disappeared. Everyone was happy except myself. First because I was disbelieved, and secondly because the hormonal test was not done. Six months later there was fever again and the lump reappeared. This time I insisted on a hormonal test. It was done, and found to be negative. I persisted with the diagnosis and insisted on an orchidectomy, and suggested that the lump in the abdomen was an enlarged lymph node causing compression of the ureter. Orchidectomy was performed with due precautions, unfortunately there was an associated hernia also. This necessitated some dissection and was responsible for the events that followed. Prior to operation, the chest was X-rayed and found to be normal. On the completion of the operation, there was a rigor. It was attributed to the glucose given intravenously. Blood count showed the W.B.Cs to be 9,000 per c mm. For several days there was a swinging temperature, normal in the morning and rising in the afternoon. The patient otherwise felt fit, ate well and slept well. The wound healed rapidly except at the lower end of the scrotal incision, where a drainage tube had been inserted. From about the third day, he developed a cough of a most distressing type. Codeine failed to give relief. I suggested skiagraphy of the chest, a secondary nodule in the left lung was already visible. Irradiation was started over the abdomen and chest. The temperature came down, cough disappeared, the nodule in the lung got smaller, the patient put on weight

and looked the picture of health. Within 5 months, he had fever again with a rigor. A persistent cough reappeared. He was re-x-rayed. There were other secondary deposits in the lung. The lump in the abdomen did not reappear. Intensive irradiation failed to give relief to this cough and he had a painful end.

Another case of similar nature had the following features. I had operated on tuberculous glands in his neck when the patient was about 20 years old. He had a fairly healthy life for 18 years. In 1942 he developed cough when in Calcutta and returned to Bombay. X-ray showed enlarged hilar glands. Some months later a mass of the size of an orange appeared in the abdomen about the level of the umbilicus. This was diagnosed elsewhere as tuberculous. Under X-rays, the lump in the abdomen disappeared. Cough cleared up. Hilar shadows cleared. The cough and the lump reappeared after 6 months. X-ray treatment was repeated with great benefit. In December 1943 he came to me for an increasing swelling of the right testis. This was diagnosed as malignant. He gave a history which was very suggestive. He had an undescended testis at first. It used to come down and go up. For some years it had come down and remained there. Only recently he noticed a gradual enlargement. Incidentally, some cases of testicular neoplasms give all the signs and symptoms of a strangulated hernia.

#### MODERN VIEWS ABOUT TREATMENT

The treatment available is —(1) Orchidectomy, (2) Radical operation, (3) Irradiation, (4) Irradiation and Surgery.

Radical operation is regarded by many as useless and those few who see some virtue in it are uncertain when to use it. With simple orchidectomy, the survival rate for 6 years was 4 per cent. Results improved after the institution of radical operation in selected cases i.e. cases without clinical evidence of metastases. With improved irradiation technique, the 5 years survival rate has been brought to 40 per cent. This is a great improvement on the results of radical operation.

For practical purposes it is best to divide patients with a positive hormone test into 2 groups.

(I) Cases without clinical evidence of metastases

(II) Cases with clinical evidence of metastases

#### Group I

Without Metastases (1) Castrate

If hormone disappears within 2 weeks and histology shows radio-sensitive tumour—prognosis is good. Look for reappearance of Prolan A and irradiate the abdomen.

(2) Castrate

Hormone disappears in 2 weeks but histological structures show radio resistance. Do a radical operation. Prognosis fair.

(a) Castration

Hormone does not disappear. Irradiate over regions of secondaries. Hormone diminishes or disappears. Persevere with irradiation.

(b) Castration

Hormone does not disappear. Irradiate. Hormone still does not disappear. Radical operation. Prognosis poor.

#### Group II

Patients with clinical evidence of metastases

A Those in good physical condition

(1) Irradiate. Metastases and hormone diminish or disappear. Prognosis fair.

(2) Irradiate—no diminution of metastases or hormone. Prognosis poor.

B Anaemic or cachectic patients—hopeless



In a general way it may be stated that radio-resistance or sensitivity is ascertained by employing irradiation. A biopsy is not advisable in the presence of metastases. In a general way it may be stated that the more radio-resistant the tumour the greater the necessity for more prolonged and less intensive irradiation. With radio-sensitive tumours like seminoma and embryonal carcinoma with lymphoid stroma it is desirable to employ maximum doses in the shortest period of time.

In a personal talk, Prof. Khanolkar informed me that Zondek now in Palestine found that in hot months, even the pregnancy test is unreliable. Hence this factor must be paid attention to, in the summer months in India.

#### DISCUSSION

Dr. Jal Paymaster said: "Within a period of three years from 6,500 cases recorded, we have seen 25 cases of testicular tumour. We have some sort of histological evidence of the nature of the tumour only in 22 cases. Side: The right testicle was affected in 9, the left in 14 and 2 abdominal testicles were involved. Age: The average age was 30 years, the youngest 15 months old, and the oldest 37 years.

There was a history of trauma in 19 out of 25 cases. The symptom of painless swelling was present in 16 cases out of 25.

We classify the testicular tumours into adult tumours, mixed tumours, embryonal tumours or carcinomas including seminomas and chorionic carcinomas.

In the cases we have treated, we had Adult—2, Mixed—1, Embryonal—17, and chorionic—2.

*Treatment* We divided them into two groups. Cases with metastases and cases without metastases. It is in the group of cases without metastases that the diagnosis is very important. In such cases we feel the A-Z test is of the greatest importance. If negative, it certainly excludes tumour. If under 500 mouse units per litre the testicular swelling is either an inflammatory condition such as syphilis, tuberculosis etc. or it is a teratoma of the adult type. If above 500, then it means we are dealing with a rapidly metastasising tumour of the testis. In cases where an A-Z test is negative or below 500, we are inclined to wait for a couple of weeks and very carefully watch the size and nature of the swelling. A repetition of the A-Z test is done in 3 weeks time, and if no improvement is seen then an orchidectomy is done and the specimen subjected to very careful histological examination, and a thorough course of post-operative radiation is given.

There is one school of thought that believes firmly in thorough pre-operative radiation, whatever the nature of the testicular tumour, while there is another which believes in removing the tumour first, subjecting it to thorough histological examination and then giving post-operative radiation. We, at the Tata Memorial Hospital, hold the latter view.

We feel that the earlier we remove the source of the metastasis from the body, the better it is for the patient and secondly, we have the histological proof of the nature of the tumour which guides us about the post-operative radiation. Those who believe in pre-operative

radiation, claim much better 5 years results, but they do not possess histological proof of the nature of the tumour because they state that frequently when they remove the testis after radiation, they find no evidence of disease, and the whole mass gets converted into a disintegrating haematoma.

**Results.** Out of 25 cases, only 18 cases have received treatment at our Hospital. Out of the 18 cases—6 cases had orchidectomy done outside. Those were mostly military patients referred to us for post-operative irradiation. Only 2 are followed up. One is without evidence of disease for 24 months. The other is well for 9 months to date. Out of the remaining 12, only 2 cases came to us without evidence of any metastasis. Orchidectomy was done on both of them.

- (1) A baby of 15 months—Histologically it was a mixed type and had post-operative X-ray. But the child died after 5 months with metastasis in the abdomen.
- (2) A man of 70 years—histologically, an embryonal type. This patient had post-operative X-rays and was well and without disease for the past 8 months.

The rest of the cases are late problems and have received only palliative X-irradiation."

**Dr A V Baliga** described two cases of testicular tumour which were associated with a clear effusion in the tunica vaginalis.

The first was a case of seminoma in which orchidectomy was performed. The patient developed paraplegia from a secondary deposit in the spine, 7 months after operation, in spite of post-operative X-irradiation. In the second case, a radical orchidectomy was attempted, but the adhesion of the secondary glandular mass to the inferior vena cava, made a total extirpation impossible, and a partial operation was performed. All his cases of testicular tumour had died of metastases, in spite of post-operative X-irradiation after orchidectomy, and he made a plea for the more frequent adoption of radical operations, particularly if the laboratory investigations indicated a comparatively radio-insensitive tumour.

He described a case of adult teratoma of the testis, in a boy of 7, which had been present from birth and in which a radiogram of the scrotum showed bone and probably teeth in the testicular lump. This was probably a non-malignant tumour conforming to Ewing's (uncommon) group of Adult Teratoma.

**Dr E J Borges** first referred to the case of an adult teratoma of the testis whose X-ray picture was demonstrated by Dr Baliga. He said that these adult teratomas are cured by a simple orchidectomy and do not require a post-operative course of Deep X-rays.

Referring to the fact mentioned by Dr Cooper that in one of his cases the Ascheim-Zondek Test was positive but orchidectomy revealed a tuberculous testicle, Dr Borges mentioned that a positive Ascheim-Zondek Test alone is not enough but a quantitative estimation of the hormone has to be done, as it has been found that even inflammatory conditions of the testis sometimes give a positive test though the amount of hormone is always under 500 mouse units per litre.

He referred to Dr Cooper's observation that in most of his cases there was some history of an imperfectly descended testis and mentioned that there was no doubt that an imperfectly descended testis was more liable to malignant change. In this connection, he had not been able to make up his mind whether an abdominal retained testis should be removed in every case, as the chance of malignancy supervening in any particular case was not very great. He would like to know the opinion of the surgeons present on this point.

**Dr K. G. Munsiff** quoted four cases of testicular tumour from his private practice, one of which presented unusual features. A young man of 30 years was referred from Cutch with a diagnosis of polyserositis, which had been confirmed by exploratory aspiration. On admission, there was a massive ascitic effusion, but there was no fluid in the pleural cavity, either clinically or radiologically. The case was diagnosed by the attending physician as one of tuberculous peritonitis and treated as such, without any benefit. When the speaker first saw the case, he noticed an absence of the right testis in the scrotum and the presence of a right inguinal hernia. He thought of the possibility of a testicular neoplasm being responsible for the ascitic collection, especially as a distinct mass was palpable in the lower abdomen and pelvis. An exploration was advised, and on its being performed, a month later, a large testicular tumour was detected, together with haemorrhagic fluid in the peritoneum.

**Dr G. M. Phadke** asked whether Dr Cooper had encountered any cases of malignancy supervening on an imperfectly descended testicle, brought down to the scrotum by operation.

**Dr V. R. Khanolkar** in his concluding remarks said that the clinical aspects of the subject had been very lucidly dealt with by Dr Cooper in his paper and in the discussion which had followed it. He had therefore nothing further to add to that admirable exposition. He would however like to say a few words about his own experience regarding the A-Z test in the diagnosis and treatment of testicular tumours. The first essential condition regarding any laboratory test was that one should fully familiarise oneself with what was to be expected from a particular test, before evacuating its merits or demerits. The A-Z test like all laboratory procedures had a much greater value when it was positive. In discussing the value of the A-Z test, it should be ascertained that it was the A-Z test which had been performed and not any modification of it. Dr Khanolkar said that he had an opportunity of studying the test as it was carried out at the Memorial Hospital in New York under the direction of Dean and Fergusson, and that at the Tata Memorial Hospital, the test was carried out exactly according to that method. When people talked of A-Z test in Bombay, they usually meant a qualitative Friedman test on rabbits or some modification on rats. This originality was commendable but was out of place when reliance was to be placed on the quantitative A-Z test. There was the further danger of getting false positive reactions in rabbits in tropical climates. It was recently pointed

out by Zondek<sup>1</sup> that rabbits were not suitable animals for quantitative determination of prolan in the sub-tropical climate of Palestine. He found that follicle haematomas developed spontaneously in these animals by climatic changes, "specially in spring and autumn by the Sirocco (dry east wind)". He also noticed a decreased sensitivity towards prolan in the winter. It was therefore urged that for a diagnosis of testicular tumours, the quantitative test as prescribed by Aschheim and Zondek should be insisted upon. It was his experience that when the test was carried out with meticulous care, it became a very useful adjunct to the clinical study of these tumours. The test gave results which were closely parallel to the rapidity of growth and the degree of radiosensitivity of these tumours. When the test was repeated it supplied a useful criterion for a prognosis of these tumours after adequate treatment. The only change he would suggest in the standard technique would be in the method of expression of results. The quantity of urine excreted in Bombay varied considerably from individual to individual, and in the same individual at different seasons of the year. He therefore expressed his results in the quantity of hormone excreted in 24 hours rather than per litre of urine. There was one other observation which he thought he should make even at the risk of being wearisome. At the Tata Memorial Hospital, many patients were referred for radiation therapy after the surgical removal of the tumour elsewhere. There could be no objection to this procedure except that the extirpated tumour had not been subjected to thorough histological study. This he thought was a serious matter so far as the patient was concerned. No specimen however innocent it may be in appearance should be discarded without a careful and exhaustive study by a competent histologist. He was convinced that every patient deserved the best treatment that was available in the locality as a result of the combined effort of the surgeon, the radiologist and the pathologist.

Dr R. N. Cooper replying to Dr Phadke's question said that he had not met with any case of a testicular neoplasm developing in a testis on which an orchidopexy had been performed.

## Clinical Conferences

### AT THE TATA MEMORIAL HOSPITAL, BOMBAY

*Conf on 14-4-44*

A patient with a chronic lung abscess treated by lobectomy was presented by Dr. E. J. Borges. (†5593). A 22 year old lad was brought by one of our patients with an 18 month's history of cough and foul expectoration. Onset was with high fever and pain in the chest. Exploratory needling was done at Goa but no pus was found. After one month the fever subsided but foul expectoration had persisted. Phrenic avulsion had been performed at Miraj in January, 1943, with no improvement. He came to us in November, 1943 and was diagnosed after improvement. He came to us in November, 1943 and was diagnosed

(1) Zondek, Bernard, — Jour Obst & Gyn. Brit Emp 49: 397, August, 1942

after investigation, as a chronic lung abscess with surrounding fibrosis. As both the patient who brought him, and the boy himself, insisted on being treated at this hospital it was decided to drain the abscess and this was done in November, 1943. For fear of opening into a normal pleural cavity a rather conservative operation was done though it would have been better to have excised a greater segment of the chest wall overlying the abscess. After this the patient stopped expectorating and improved remarkably in his general health, but the sinus persisted, and though the abscess cavity remained empty, the walls would not come together. After 4 months it was decided that the best treatment was a lobectomy, as the abscess was at the periphery of the lower lobe. This was done on the 20th March, 1944. Difficulty was met with from adhesions between the lobes, and adhesions to the diaphragm and the chest wall. The sinus, plus a segment of the adjacent chest wall, were resected with the lower lobe. Two lung tourniquets were used before severing the pedicle. The chest was closed with drainage. Post-operatively he developed a bronchitis, a mild basal empyema and a bronchial fistula. The latter two are said to be invariably met with after lobectomy for septic conditions and clear up in a few weeks. The patient was shown and was well, and able to move about. He had a sinus which was rapidly healing up. Dr Borges stated that this operation would not have been successful without the invaluable assistance of Dr Sircar's anaesthesia.

Dr K. P. Mody pointed out the value of short-wave therapy in acute abscess of the lung. Dr A. V. Baliga said that in an abscess of the lung one was often agreeably surprised to find a persistent abscess heal up if bronchoscopic suction was persisted upon, though he would not think that it would have done so in the case presented. Dr K. Narvekar drew attention to the two types of lung abscesses, the putrid and non-putrid, which clinically behaved and should be treated, differently. Dr D. J. Jussawalla on discussing Dr Borges' case of lobectomy, mentioned two points of importance in the surgical technique of the operation. The tourniquet method of ligating the hilar stump had no doubt, simplified the operation to some extent but in a certain number of cases, tuberculous infection was known to have flared up after the operation, presumably on account of the crushing of old tubercular nodes in the hilum. In a certain number of cases, a mediastinal empyema had resulted through the same cause. In carcinoma of the lung this tourniquet cannot be used, as each individual structure had to be identified and tied separately. This was particularly indicated in a total pneumectomy as a mass ligation in such cases involves the risk of leaving behind some amount of cancerous tissue at the hilum.

Dr D. J. Jussawalla presented a case (†6321) of extensive cancer of the thyroid with lymphatic node metastasis. This case was shown at an earlier conference. The patient was subsequently operated upon, and the thyroid gland was removed en bloc with a radical neck dissection, including removal of the internal jugular vein and the sternomastoid muscle on the left side. An interesting point observed was that whereas the tumour appeared to originate in the right half of

the thyroid, most of the secondary nodes were found on the left side. The left recurrent laryngeal nerve was isolated and preserved, the right nerve was removed as it could not be freed, off the tumour mass. The patient stood the operation excellently, in spite of a low Hb of 48 per cent and an RBC count of 2.4 millions. This anaemia had proved refractory to the usual line of treatment for three weeks, and it was thought that no more time should be wasted in trying to improve the blood picture. The histology of the tumour was reported as giant cell carcinoma of the thyroid. Dr Jussawalla commented that this was the relatively rare type of cancer of the thyroid occurring in about 11 per cent of the total thyroid cancer group. They were unfortunately radio-resistant. Finally, a plea was made for early removal of any nodular mass in the thyroid soon after its appearance, as most cases of cancer in this gland originated in a previously observed benign adenoma (about 90 per cent being the figure mentioned).

*Conf on 21-4-44*

Dr V R Khanolkar presented the pathological material from a relatively rare case of a deep seated **Epidermoid Carcinoma** of the female breast. The patient (†6334) was a 52 year old woman with history of a lump in the left breast which she had noticed for one month. A physical examination revealed a firm, nodular, lobulated mass lying embedded in the upper half of the mammary gland on the left side. It was neither adherent to the skin, nor fixed to the chest wall. The axillary lymph nodes were enlarged. The opposite breast showed no abnormality. The specimen after mastectomy showed an ovoid tumour measuring 4 cms in its long axis. On cutting through the tumour area a small cyst with a smooth wall was seen with an adjacent greyish firm round nodule about  $1\frac{1}{2}$  cms in diameter lying close to it. The tissue from this area bulged out above the cut surface and presented a shaggy filamentous appearance. The microscopical examination showed three distinct areas (1) The circular tumour area which consisted of a central debris of keratinised tissue in sheaves and whorls without much cellular material, a peripheral layer of pavemented columnar and cuboidal cells, with ovoid and hyperchromatic nuclei. An intermediate zone of large clear polygonal cells, with pale vesicular nuclei containing one or two big round acidophilic nucleoli. The borders of these cells were distinct with many of them showing delicate protoplasmic intercellular bridges. The whole picture conveyed the impression of a circular cavity packed with long degenerating papillary processes lined with squamous stratified epithelium. (2) The cystic space was lined by discontinuous sheets of compressed epithelial cells 5-6 layers deep. These cells showed dense staining nuclei and presented different stages in the progressive squamous metaplasia of the lining of a distended duct with a few blunt epithelial protruberances into the lumen. (3) The intervening zone showed strands and columns of tumour cells infiltrating into the fibrovascular connective tissue. These clumps of tumour cells showed differentiation into polygonal cells and keratinised scales. There was a stroma reaction, mainly made

up of plasma cells and lymphocytes. The histological appearance left no doubt regarding the diagnosis of a squamous carcinoma of the breast. Dr Khanolkar said that this was the fourth case which had been reported as squamous carcinoma in the material received in the department during the last three years. He said that he had reviewed the material carefully and re-examined the slides again and felt doubtful if any of those three cases were squamous carcinomas. He described those cases (†193, 1682, 3729) and gave reasons why he was led to doubt the original diagnosis. The frequency<sup>1</sup> of squamous carcinoma had been given as ranging between 0.5–2 per cent. It originated as a result of a metaplasia of the lining epithelium of the larger ducts. The cells proliferated, distended and broke through the ducts into the surrounding stroma. These tumours appeared to possess a high grade of malignancy and gave rise to early and widely scattered metastases.

Mr M V Raghunath gave a brief review of the work that was being carried out in the Pathology Department, on blood groups in relation to cancer. He said that at the suggestion of Prof D D Kosambi the blood groups of all patients who were admitted to the hospital were determined and recorded. Blood group data from non-cancerous patients in adjacent hospitals were collected. The largest group of a single type of cancer with adequate control was supplied by comparing the blood groups in Deccani women having cancer of uterus with blood groups in Deccani women who were admitted for labour at N W Maternity Hospital as controls. The results were as follows:

BLOOD GROUPS IN DECCANIES

Group	Normal Individuals (682)	Cancer cases (100)
A	28.9%	28.0%
B	28.4	34.0
AB	7.8	4.0
O	39.4	34.0

The data had not so far been subjected to a statistical analysis for finding if there was any significant difference between the two populations.

Dr M V Sirsat discussed a case of *Osteitis Fibrosa Cystica* (†6545). A male patient aged 18 years was admitted to the hospital on 17-3-'44, with a history of limping for the last one year but no pain. On examination it was noticed that swelling measuring 15 x 10 cms was situated on the outer aspect of the left thigh. It was hard to feel. There was no shortening or deformity of the legs. X-ray examination showed an appearance of rarefied areas separated by intervening septa. At the time of operation, the entire tumour was scooped out and bone grafts were kept firmly in the cavity of the cyst. The limb was put in the plaster. The histological examination of the wall of the cyst showed a structure of localised variety of *osteitis fibrosa cystica*. There were seen cystic spaces surrounded by fusiform cells. The nuclei of these cells were ovoid or pointed in shape and uniform in size. Multi-

<sup>1</sup> Foot, N. C. and Moore, S. W.—A fatal case of deep-seated epidermoid carcinoma of the breast with widespread metastasis. *Am. J. Cancer* 34: 226; 1938.

nucleated giant cells were detected. Clear intercellular material separated the tumour cells. Dr Sirsat said that this condition should be distinguished from two other types of similar lesions with which it was often confused. One was the generalised type of osteitis fibrosa cystica and the other a Benign giant cell tumour.

The generalised form was the one described by von Recklinghausen and was associated in majority of cases with overactivity of the parathyroid glands. The biochemical changes are striking. There is a rise in blood calcium but the phosphorus remains low. In benign giant cell tumour the giant cells and stroma cells form the essential diagnostic criteria. The blood calcium and phosphorus remain at the normal level.

The localised variety of osteitis fibrosa cystica bore no relation to any of the above conditions. Many theories regarding the genesis of this tumour have been suggested. Histologically the localised form showed in most instances a bone destructive process which explained the cavity formation. The examination of the section through the wall of the cyst showed spindle shaped cells and fibroblasts. An abscess wall and the periosteum overlying an ossifying hematoma were very often mistakenly diagnosed as osteitis fibrosa cystica on the basis of the histological appearance alone when unaccompanied by the radiographic and other clinical data.

## *a review*

## INFECTIVE HEPATITIS

by F. O. MacCallum, B.Sc., M.D.,

Though jaundice had appeared in epidemic form on a number of occasions in different countries in the 19th century, it was not till 1912 that Cockayne in England pointed out that there seemed to be two forms of infective jaundice, one characterised by a high fever and considerable mortality, the other almost afebrile and relatively benign. The severe form, first described by Weil, was proved to be caused by a leptospira. The benign form consists chiefly of cases of infective hepatitis which may be epidemic, endemic, and perhaps sporadic. There are probably also a small number of cases of true catarrhal and obstructive jaundice, the result of blockage of the bile duct due to a mucus plug or inflammation of its wall. Certain groups of workers, especially in Germany, consider that there is a clinical distinction between these two types of the benign form, and that the catarrhal type is responsible for sporadic cases. This would appear to be a debatable point which can only be solved by an extremely large number of liver biopsies on such cases, or by isolation of a causative agent and an accompanying diagnostic laboratory test.

### DISTRIBUTION OF CASES

The disease usually runs a benign course with the majority of cases occurring in children of school age. However, from time to time outbreaks of a more severe type occur which extend to the adult population and may result in an increased number of fatal cases as reported by Wallgren (1930) and Bergstrand (1930) in Sweden.



As in previous wars, this disease has become widely prevalent in the combatant forces Van Rooyen & Gordon (1942) and Cameron (1943) have described a large number of cases from Libya, Egypt and Palestine Dietrich (1942), Gutzert (1942), Stuhlfauth (1941), Jacobi (1942) and others have described large numbers of cases among German troops in Occupied Countries and on the various fronts Ford (1943) has given a good account of an epidemic of hepatitis in the civilian population of England

#### CLINICAL PICTURE

The signs and symptoms of individual cases and groups of cases may vary considerably, but a composite picture of the disease would be somewhat as follows The onset is frequently marked by fatigue headache, loss of appetite and an urticarial or morbilliform rash Fever, nausea and vomiting, diarrhoea or constipation, and an abdominal pain or a feeling of fullness may occur, as may generalised aches and stiffness of the joints After these symptoms have lasted for a varying period, jaundice as a rule appears Alternatively, there may be a free interval before its onset, or it may be the first observed sign Some cases may have a transient biliuria and never become clinically jaundiced The patient usually feels much better with the onset of jaundice In the vast majority of cases the jaundice disappears in one to four weeks, but a few cases may progress to a sub-acute liver atrophy and an occasional one may die with acute yellow atrophy

#### AETIOLOGY AND MODE OF TRANSMISSION

Observations of short and established single exposures made by Booth & Okell (1928) and Pickles (1939) indicate that the incubation period is about 20 to 40 days The possibility of a longer period under certain conditions must, however, be considered, because cases have been seen in which it appeared that a latent infection had become manifest when the patient's resistance was lowered by another illness or extreme fatigue The mode of spread has most frequently been considered to be by droplet infection Some observers in Scandinavia and Germany have favoured the oral route by contaminated water, etc., but no evidence indicating milk, water or food as the source of infection has been forthcoming in Great Britain

In recent years, cases of clinically similar jaundice have occurred following the use of certain batches of measles convalescent serum, adult serum, mumps convalescent plasma, and yellow fever vaccine which contained serum from apparently healthy adults In 1937 Findlay & MacCallum first described cases of jaundice occurring in individuals two to seven months after they had been inoculated with certain batches of yellow-fever vaccine Human serum from normal donors was used in making the vaccine, and hyperimmune serum from recovered cases was given with the vaccine in the majority of instances None of the sera used could be traced to a donor known to be suffering from jaundice at the time he was bled All sera were preserved by the addition of 0.2% tricresol, and stored in sealed ampoules

at 2° C Before use the serum was passed through a Seitz K filter and later all sera were heated at 56° C for half an hour In 1939, following a close check of all stages in the process, Findlay, MacCallum & Murgatroyd came to the conclusion that the source of the icterogenic agent was probably the human serum which had been introduced into the yellow-fever virus tissue cultures from which the vaccine was made and possibly propagated there along with the yellow-fever virus This has not been confirmed as yet Similar incidents on a much larger scale have been reported by Soper & Smith (1940) and Fox, Manso, Penna & Para (1942) from Brazil, and by the Surgeon-General's Office of the U S Army in 1942 In most instances the disease runs a benign course, similar to that seen in infective hepatitis, but a small number of fatal cases have occurred It has been established that the condition is not a form of yellow-fever itself At the present moment the most striking difference between the two conditions is the apparent lack of secondary cases among people exposed to individuals with post-vaccine jaundice The interval between inoculation and onset of illness is also considerably longer than the usually accepted incubation period in infective hepatitis, but this may be related to the route of infection The most popular view is that serum from an individual in the incubation stage of infective hepatitis has been included in the pool of serum used on these occasions However, until the infective agent is isolated, the possibility of the disease being caused by some other factor present in certain human sera cannot be ruled out

Since the introduction of arsenical drugs for the treatment of syphilis, many different clinics have reported cases of jaundice occurring at varying stages of the treatment In the early days some of this may have been a true arsenical poisoning from impure batches of the drug However, in later years, retesting of supposedly incriminated lot by animal toxicity tests did not support this hypothesis Since the last war interest in arseno-therapy jaundice has not been as great as it should have been, but is now revived because of the effects of this disease on military personnel (Mitchell, 1943) Many venereologists consider the problem has been solved by the use of less toxic preparations such as mapharsen (m-amino-p-hydroxyphenylarsenoxide) On the other hand, many pathologists favour the possibility that as a result of drug treatment the liver is rendered more susceptible to the hypothetical virus of infective hepatitis Another possibility, as mentioned by Bigger (1943) and others, is that infective blood from one patient is carried to another because of imperfect sterilization of syringes

Anderson (1937) claims to have infected pigs with materials from cases of infective hepatitis in Denmark, but unfortunately a porcine hepatitis was present in the country at the time so that the results are difficult to assess Siede & Meding (1941), and Siede & Luz (1943) have reported transmission to developing chick embryos Other workers such as Hoyle (1943), have failed to confirm any of these

results or transmit the disease to any laboratory animal. However, Dresel, Meding & Weineck (1943) have recently reported the infection of canaries by inoculating duodenal juice and urine from humans in the preicteric phase of the disease. Experiments with human volunteers have been carried out on a small scale by several workers. Voegt (1942) has reported successful transmission by oral administration of small amounts of duodenal juice and subcutaneous and intramuscular injection of serum and blood from cases of infective hepatitis. Cameron (1943) injected serum or whole blood subcutaneously in 7 volunteers. Of the 6 he was able to follow, all developed jaundice one to six months later. Recently Oliphant, Gilliam & Larson (1943) have been able to show that the serum of a group of individuals who had developed jaundice following inoculation with icterogenic batches of yellow-fever vaccine, was capable of producing the disease when inoculated subcutaneously into a second group of individuals. A further passage to a third group of normals was possible with the serum of those who developed jaundice in the second group. Serum taken in the preicteric stage was icterogenic, but that taken from one patient 2½ months after the jaundice failed to produce jaundice in 15 inoculated volunteers. The icterogenic agent was not inactivated by heating at 56° C for 30 minutes, but following exposure to ultra-violet radiation of 2650 Å for 1 hour and 2537 Å for 1½ hours, an icterogenic lot of vaccine failed to produce jaundice in 10 volunteers. As in all previously reported experiments attempts to infect laboratory animals, including the Syrian hamster (*Cricetus auretus*) and cotton rat (*Sigmodon hispidus*), were unsuccessful. In an attempt to prove the infectious nature of so-called yellow-fever-vaccine jaundice, Findlay & Martin (1943) collected nasopharyngeal washings from three patients thought to be suffering from this disease. The washings were instilled intranasally in three supposedly normal individuals, each of whom was said to have developed jaundice after 28, 30 and 56 days respectively. If the yellow-fever-vaccine jaundice is a form of infective hepatitis, it is remarkable that there have not been reports of large numbers of cases of the disease among individuals exposed to these cases. A great deal more work is necessary before any conclusion can be drawn from these experimental results.

Aspiration biopsy of the liver as practised by Iversen & Roholm (1939) and by Dible, McMichael & Sherlock (1943) is a great achievement, helping to clarify our understanding of the underlying histology which had previously been based almost entirely on post-mortem material of cases which developed acute atrophy. The work of Dible and his colleagues in demonstrating a common picture in infective hepatitis, arsenotherapy jaundice and so-called serum jaundice, is especially interesting.

Until the causative agent is isolated and the disease transmitted to a laboratory animal, or some diagnostic laboratory test is discovered, the question of mode of transmission and aetiological relationship of these various conditions must remain largely theoretical.

# The Indian Physician

4 VOL III NO 8

AUGUST 1944

WHOLE NO 32

*Let us remember*

## CAUSES OF DEATH OF FAMOUS MEDICAL MEN AND PRACTITIONERS

LUDWIG ASCHOFF

Freiburg

*Any person who wishes to devote himself to learning must possess a strong healthy body and a healthy mind. I think this matter is so important that it deserves the attention of the Minister of the State*

J Ch G ACKERMANN 'On the diseases of the learned' Nurnberg, 1777 p 11

As can be seen from the two recent issues of Med Klinik, the postal authorities of foreign countries have included some doctors among the people selected for portrayal on their postage stamps. This is probably one of the best methods of signalling their worth towards the welfare of the people.

The following few lines have been put together particularly because I have had an opportunity of ascertaining the cause of death of some famous physicians by being present, either, at their bedside, or at the autopsy table. I have included medical colleagues who were famous for their clinical practice along with notable non-practicing physicians for obvious reasons. The published obituaries particularly those which have appeared in Munch Med Wschr have been helpful in gleaning information about men who have lived before my time on whose death-bed I have been unable to attend. I have also consulted the historical essay of H Vierordt (Med Klin Nos 17, 18, 19 1915), and his monograph on "The causes of death in medical profession" which includes the period covering the ancient medicine.

I have already published elsewhere a short report of the last days of H E The Hon Dr Baumler without mentioning his name. I was with him two days before he died in his 97th year. On that occasion he was lying on a sofa, and evinced a keen interest in our affairs, our outings and our health. I did not notice anything particular in him except marked tiredness. That was the reason why two days later when I heard of his death just before my class, I told my students during the lecture that to my knowledge Baumler was the only case in which a natural death had terminated a person's life. I was therefore very much surprised when the next day as a result of his expressed desire I performed a post-mortem examination on his body and found

numerous secondary deposits of an osteochondrosarcoma of the thyroid scattered in many viscera. My astonishment was even greater when I found an acute inflammation, of several days' duration in one of his lungs. I had to confess to my students that even in this very aged man death did not close in naturally but followed some morbid process. I also added that so great a diagnostician as Baumler was hardly able to diagnose his own condition because just a few days before his death he had said to his wife "I feel perfectly fit, only just a little tired."

I experienced another surprise at the autopsy on Naunyn which was undertaken at Baden Baden following the wish of the deceased in his home. He was inclined to think that he was suffering from the cancer of the intestine and that his cardiovascular system was perfectly sound. At the post-mortem it was established that death had supervened an acute softening of the heart muscle leading to a rupture of the heart wall and a consequent fatal bleeding in the pericardial sac. This softening of the heart muscle had resulted from an extensive sclerosis of the coronary vessels. Naunyn had not felt any signs during his lifetime which could have led him suspect his condition. He was not even conscious of the old softening of his heart muscle. The fatal tear in the heart occurred one morning as he jumped in a hurry out of his bed. I think I may attribute this sudden action to a moderate retention of the urine due to a cancer which I found in the prostate, and not in the bowel as was erroneously believed by Naunyn on the occasion of an attack of appendicitis. The appendix had been removed previously and had proved to be inflamed and not cancerous. It is worth remarking that besides these lesions all the other organs in his body were perfectly healthy and even young which was confirmed by the presence of real lymph follicles in his bone marrow.

B Kronig was laid up for a few weeks with heart attacks. At the post-mortem examination I found a marked narrowing at the mouth of the coronary vessels. He expired during a very painful attack of angina pectoris. Similarly I had to examine Pankow following his predecessor Erich Opitz who had succeeded Kronig. Opitz had succumbed to an embolism following a motor car accident in Garinisch and Pankow to a bronchogenic carcinoma which had given rise to multiple secondary deposits in several organs. It seems that our colleague Pankow expired as a result of the effects of these deposits.

The other physicians and medical men who fell a prey to heart disease may be mentioned briefly. Morawitz, Sternberg, Walkhoff, Fulleborn, Perthes, Tarassewitsch, Lubarsch, Braun, Goltz, R. Koch, Weigert, Herxheimer (the pathologist), E. Lexer, Eppinger (the pathologist), Ulric Quensel, Chiari (Pathologist in Strassburg). I have here at hand, their obituary notices and I have selected only a few names. I shall revert to this subject of heart disease in medical men later.

The following succumbed to an apoplexy: Julius Arnold, Tandler, the senior, Spatz, Watzold, Kallius.

Many medical men have given their life in the pursuit of their

profession So much homage has been rendered to the radiologists who have died of cancer that it is not necessary to add to it However, the name of Holz knecht should receive the first place The names of French radiologists who were victims to their work are given in Haubolds book on Cancer Campaign in France The names of the German and foreign radiologists will be found in the Book of Honour of Roentgenologists and Radiologists published by Hans Meyer in 1937

Medical men are particularly exposed to infection and to blood poisoning Bach died of an erysipelas which he contracted during his work The pathologists are very liable to get infected while working with germs or examining dead bodies It is in this manner that we had to lament the loss of Schmorl who died of a septic infection in his 70th year We were equally touched by the death of Benda who along with many other pathologists lost his life by getting infected in the course of their work Here are mentioned the names of some of the pathologists Jager, Koppenhoefer, Reinhardt, Krischner, Hammar, Stumpf, Radecke Jun

An almost as large a number of doctors have died of accidents or war wounds I mention only v Gaza, Wiedenburger, Gamper, Tilp v Beerenberg-Gossler, Thies, Dibbelt whom I wanted to visit or had visited shortly before they laid down their life in the World War H I Arndt died a voluntary death

The number of doctors who have been victims of tuberculosis is relatively small I mention first of all Otto Naegli because I have intimate recollections of his illness and death Of the older physicians one should mention Laennec and v Graefe Of the pathologists Ribbert died of consumption due to the privations caused by the war, as also Albrecht slightly before him W Toldte also fell a prey to this illness

About the same number have died of cancer The following may be mentioned Fibiger, Buchner, Henle, Key, Dohi

Many doctors have died of an inflammation of the lung I name only the following Sommer, Spielmeyer, Flemming, Kollé, v Lenhossek

The other causes of death are relatively rare O Klotz died of leukaemia, Hufeland of a urinary bladder disease and Hauser of the complications of appendicitis A constricting goitre was found to have caused the death of Schonelein v Merkel died of pyelitis and Siegenbek van Heukelom of Addison's disease v Rindfleisch slowly passed away as a result of a softening of the brain following on an atherosclerosis

This short survey leads to the recognition of at least one fact that heart disease and paralytic stroke which are both of them traceable to atherosclerosis are between them responsible for the largest number of deaths in doctors This accords with the observations of H L Smith (Collected Papers, Mayo Clinic, 1936) that deaths due to coronary sclerosis and its sequelae are twice as common among doctors as in other academic professions One must however take into consideration the fact that medical men on an average attain a relatively long age Smith has reckoned that doctors have an expectation of 52.8 years as against 52.2 years for clergymen Against this small difference it is found that the incidence of death due to coronary disease is only half as great in bankers though their expectation of life is the

same (52 8 years) It therefore becomes necessary to consider carefully the effects of a profession which attacks the heart in doctors, and spares the cool and calculating bankers In any case the above instances—which are far from being statistically exhaustive—support the assumption of H Smith that medical men are particularly prone to suffer from coronary sclerosis and its complications

**Translator's Note** The original article entitled "Todesursachen namhafter Mediziner und Ärzte" appeared in *Medizinische Klinik*, Berlin, on 5th May 1939 about 8 years before Aschoff's death on 24th June, 1942 Ludwig Aschoff was probably the most eminent pathologist of the last generation, and this article presents so many points of interest to an Indian physician that no apology is offered for having undertaken the translation. It is necessary to mention that an attempt has been made to convey the spirit rather than to adhere to the letter of the written word. (V R. Khanolkar)

(It may be of interest to note here the names of some of the great physicians of old who made epochal contributions to the physiology and pathology of the heart and circulation and who themselves died of Cardio-vascular disease)

WILLIAM HARVEY (1578 1637) 79: Gout; Cerebral Haemorrhage

MARCELLO MALPIGHI (1628 1694) 66 Apoplexy

WILLIAM COWPER (1666 1709) 43 Asthma, Dropsy

JOHN HUNTER (1728 1793) 65 Angina Pectoris

Hunter began to suffer from recurring attacks of Angina pectoris in 1785 He said that his life was in the hands of any rascal who chose to annoy and tease him He died following a violent disagreement at a meeting of the board of governors of St George's Hospital on Oct 16, 1793 where a colleague had directed some disparaging remarks to him A post mortem examination revealed sclerosed coronaries which were like bony tubes and widespread areas of fibrosis suggestive of healed myocardial infarction

JEAN NICOLAS CORVISART (1755 1821) 6 Apoplexy, 1815 1821

WILLIAM CHARLES WELLS (1757 1817) 60 Cerebral Thrombosis

JOHN CHEYNE (1777 1836) 59 Cataract Gangrene of the arm

CALEB HILLIER PARRY (1755-1822) 67 Apoplexy 1816

ROBERT ADAMS (1791 1875) 84 Cardiac Disease

DOMINIC JOHN CORRIGAN (1802 1880) 78 Gout Apoplexy

WILLIAM STOKES (1804 1878) 74 Paralytic Seizure

AUSTIN FLINT (1812 1886) 74: Cerebral Haemorrhage

LUDWIG TRAUBE (1818 1876) 58 Angina Pectoris Congestive Cardiac Failure

Traube suffered from repeated attacks of Angina pectoris from the age of 50 and ultimately developed Congestive cardiac failure Traube diagnosed his own disease as follows

Hypertrophy and dilatation of both ventricles with arteriosclerosis and coronary sclerosis with partial degeneration of the myocardium

PIERRE EDOUARD POTAIN (1825-1901) 76 Coronary Occlusion

HEINRICH QUINCKE (1842 1922) 80 Coronary Occlusion

WILLIAM MURRELL (1853 1912) 59: Heart Disease

MARTIN FLACK (1882 1931) 49: Rheumatic Heart Septicemia

JAMES MACKENZIE (1853 1925) 72 Angina Pectoris Coronary Sclerosis

Mackenzie had extrasystoles at the age of 40 At the age of 47 he had his first attack of cardiac irregularity which occurred after running 300-400 yards and lasted for 2 hours A tracing of the pulse taken by himself showed auricular fibrillation During the next four or five years several similar attacks occurred In 1907 he observed limitation of effort a slight feeling of constriction hardly amounting to pain in the upper part of the chest on severe continued exertion which soon ceased with rest In 1908 at the age of 55 he had his first severe attack of cardiac pain, which occurred at night when resting and lasted for two hours He also suffered from intermittent claudication on continuous walking since 1909 He had several attacks of prolonged chest pain lasting for  $\frac{1}{2}$  to 2 hours or more Death followed a severe and prolonged attack in January 1925 At his request a post mortem examination of his heart was carried out by John Parkinson, who found advanced and wide spread degenerative changes in the coronary arteries Sir Thomas Lewis and Grant examined the heart and agreed that there were amply sufficient old-standing changes at the apex of the heart to account for the first attack of pain which occurred in 1908 seventeen years before his death, and which clinically strongly suggested coronary thrombosis The numerous small patches of fibrosis suggested numerous small thromboses at different times The terminal severe attack of pain and cardiac impairment was due to the recent infarction found at the apex of the left ventricle)

N D P

# Original Contributions

## CONVULSION THERAPY IN MENTAL DISORDERS

By

N S VAHIA, M D

K E M Hospital—BOMBAY

Like the sulphonamide group of drugs in general medicine, convulsion therapy has evoked considerable interest amongst medical men dealing with mental disorders. At first tried in schizophrenia, it was received with great enthusiasm and was tried in other disorders, till it was used so indiscriminately that it came to receive severe criticism. "At the present time it can be definitely stated that convulsion therapy has achieved for itself a definite niche in the therapeutic armamentarium of those physicians concerned with mental disorders." "At the same time it has been emphasised repeatedly that shock treatment of any sort should be only a small part of the total therapy in any case of personality dysfunction."

In 1934-35 Ladislaus von Meduna, Superintendent of the Royal State Mental Hospital in Budapest, believing in a certain "biological antagonism" between convulsive states and the schizophrenic process, induced convulsions in schizophrenic patients at first by intra-muscular injections of camphor in oil and later by cardiazol. Though a large number of drugs have since been tried viz triazol, ammonium chloride, picrotoxin, inhalation of nitrous oxide and nitrogen, in the treatment of schizophrenia one can state that no drug has so far been found to be superior to cardiazol.

In 1937-38 Cerletti and Bini in Italy made use of the electric current to induce convulsive seizures in dogs and later used similar methods for schizophrenia patients. Their work was immediately taken over by many workers on the Continent, England and America, by Kalinowsky, Myerson, Shepley, Fleming, Barrera, to mention but a few.

The *modus operandi* of the convulsion therapy is much discussed because so far no one has hit upon a suitable explanation acceptable to all workers. In the opinion of Spiegel and Spiegel-Adolph, the convulsions produced in this way are due to an increase in the permeability of cellular surface films, thus facilitating an exchange of ions between cytoplasm and environment with subsequent removal of metabolic products.

On the other hand the psychological explanation offered is that the improvement is due to the patient's idea of the treatment as a sort of punishment, threat to his existence, or as death and rebirth.

On experimental grounds it is suggested that the therapeutic benefit may be caused by a destruction of nerve cells within the cerebral cortex.



There is considerable difference of opinion regarding the suitable indications for convulsion therapy. It has been found most useful in mild depressive states, involuntional melancholia, senile melancholia, manic-depressive psychosis and early schizophrenia. It has been tried in severe cases of psycho-neurosis, particularly of anxiety neurosis. It is found to be of little value in established schizophrenia with splitting of personality, hallucinations and delusions, hebephrenic forms of schizophrenia, paranoid psychosis and compulsive neurosis.

This form of therapy is contra-indicated in the presence of active or recently healed tuberculosis, arthritis of spine, fever, hypertension, arteriosclerosis, severe cardiac disease, nephritis and organic disease of the central nervous system.

In order to induce the actual convulsion, the patient is made to lie on a hard, flat non-metal table with hands and feet stretched out. He is held gently but firmly. A hard small pillow is kept under the mid-thoracic region of the spine to cause hyperextension. A cotton or gauze mouth gag is kept ready to put between the teeth during convulsion. The dose of cardiazol varies from 4 cc to 10 cc. The drug (average 5 cc) is injected intravenously rapidly and the needle quickly withdrawn. Instantaneously or after a latent period of about 30 seconds the patient loses consciousness. He gets convulsions at first tonic and later clonic. There is temporary cessation of respiration, pupils become dilated and cyanosis may occur. There may be incontinence of urine and stools, and ejaculation has been reported. The actual attack lasts for 30 to 90 seconds, but the patient remains dazed for 10 to 15 minutes longer and later sleeps on or complains of headache. The injections are generally repeated two or three times a week. The total number of injections may be varied at will. More shocks are required in cases of schizophrenia than in states of depression. Hemphill and Walter have given daily injections for 60 days or more with no ill-effect. Myerson on the other hand gives as few as possible. There is some evidence, electroencephalographic, to show that more than 10 to 12 injections may cause permanent damage to brain tissue.

For electrical convulsions, the preliminary preparations are not different. A special instrument is required to modify the current to our requirement. The instrument permits the current of voltage varying from 70 to 150 volts and 300 to 1000 milli amperes for a time varying from 0.5 to 2 seconds by means of an automatic time controller. The electrodes are applied to the skin high up in the temporal region with the use of a special paste like the one used in electro-cardiography, or with pads saturated with 20% salt solution. Shaving of the scalp is not necessary. A current of about 400 to 700 milli amperes is allowed to pass for from 0.2 to 0.5 seconds as found necessary after applying the test current. Convulsions are exactly similar except that they are less violent and the patient recovers more rapidly and quietly.

Premedication is recently practised by many workers. Bennett advises the use of curare to remove the danger of fracture, sprains,

backache etc, and hyoscine to prevent the feelings of apprehension and post-convulsive excitement Bailey, in order to reduce the strength of current required, has suggested the use of amphetamine (Benzedrine) sulphate which lowers the electrical convulsion threshold

Convulsion therapy is not without dangers Common complications are headache, nausea, vomiting, psycho-motor excitement, dislocation of lower jaw and shoulder and fractures of spine, neck of femur, humerus and scapula Rarer complications described are status epilepticus, disturbance of memory, epilepsy, subarachnoid haemorrhage, cerebral haemorrhage and even acute perforated duodenal ulcer following cardiazol therapy has been described Fatal aplastic anaemia has been reported following cardiazol shock therapy A death rate of 23 per 10,000 in cardiazol has been reported by Kinsey No deaths were reported in over 10,000 electric shock treatment by Kalinowsky

The results of treatment will depend upon the nature of illness, the duration of illness, the mode of onset, the pre-psychotic personality and the presence of precipitating factors etc It will also depend to some extent upon the interpretation of the result, since the criteria and definition of recovery, improvement, slight improvement etc, will vary with each individual At the same time while estimating the efficiency of any line of treatment for mental disorders it is important to remember that natural remissions are known to occur to a certain extent in these conditions irrespective of any treatment and special attention is drawn to this by Cobb, Gelparin and others Most of the workers have reported remissions in 70% to 80% of depressive states Good results are reported in mania Sogliani reported "Recovery" in 12 out of 15 schizophrenia cases of less than one year's duration, but in only 3 out of 55 cases of more than one year's duration Many workers have reported 21 to 80% recovery in schizophrenia of recent onset Majority of mild depressive psychosis even of several years' duration have been relieved by 3 to 8 convulsions according to Andratschke and Rogerson

Electricity is preferable to cardiazol therapy as it is more acceptable to the patient and easier to administer, the convulsions are less violent, and there is less confusion after the convulsion Vast majority of the cases show no "fear reaction" because the convulsion occurs instantaneously, and there is complete amnesia for the convulsion and some time preceding it Fractures and other complications are fewer

With a view to determine the status of convulsion therapy in mental disorders in India, I have tried to amass information on the subject from all the Mental Hospitals mentioned in the Indian Medical Review of 1938 (Major General E W C Bdadfield) Of the 17 hospitals to which a questionnaire was sent only 2 hospitals did not reply, 5 hospitals have not tried that treatment so far, 6 other hospitals have tried the treatment but for certain reasons were unable to supply any useful information,

# Case Reports

## CEREBELLAR ATAXIA

*By*

R J WEINGARTEN

M D (COLOGNE)

Principal Medical Officer Bikaner State

Cerebellar and spino-cerebellar degenerative disorders appear to be very rare occurrences in India. Elsewhere also these diseases form only a small group among nervous affections. There were, for instance, 73 cases of Friedreich's ataxia out of a total number of \*15,923 cases admitted in the National Hospital in London from 1909 to 1925. Out of a very large material, with 3,790 cases of diseases of the nervous system, seen as indoor and outdoor patients in Bikaner hospitals, I have only come across one sporadic case of this disease.

Therefore, a short account of a family with heredo-cerebellar ataxia, an even rarer affliction, seems justified.

In 1934 an Indian patient, then 25 years old, came to consult me with the following history.

Several members of his family had suffered from nervous disorders, mainly consisting of difficulty in walking and speaking, gradually leading to complete inability to move about, and incomprehensible speech. The father of the patient noticed the first symptoms in 1907 at the age of 21 and he died in 1924 from pneumonia. The patient himself had been to England in 1928 where he consulted Doctors Russel and Turner and their conclusion was "as the result of a careful examination, we were unable to discover any evidence of an organic disease of his nervous system or indeed of any of his internal organs."

Since 1929, the patient suffered from chronic rhinitis for which an operation of the turbinate was done without relieving him. Another nasal operation was performed in Vienna in 1932 and since then only occasional attacks of nasal catarrh occurred.

When I saw the patient in 1934 he had for several months observed unsteadiness in walking, particularly when descending stairs, and sometimes a tendency to fall while playing tennis. In addition, he complained of double vision in looking upwards or downwards. He is a very moderate smoker, only occasionally taking alcohol, and without any history of venereal disease. Occasional attacks of malaria had been promptly treated. The findings at that time were as follows.

Physical condition excellent. Blood pressure normal. Chest and abdominal organs without anything pathological. Intelligence above average. Memory highly developed. Movements of eyes proper and simultaneous in all directions. No nystagmus. No ptosis of the eyelids. Pupils round and promptly reacting to light and accommodation. Eye ground, vessels, discs and maculae perfectly normal. Facial

\* Neurology—Vol II page 944, by S. A. Kinnier Wilson, 1940

movements unimpaired as well as movements of the tongue and soft palate Speech slightly hesitant and slow Articulation slurred and occasionally indistinct with multisyllable words Motor power of both arms and legs fair Sensory functions on the whole undisturbed but slight difficulty in differentiating between hot and cold on the skin of the lower legs—Abdominal and cremaster reflexes present Tendon reflexes of both arms and legs very exaggerated but no clonus The arches of both feet are normal with a sharp plantar reflex of the big toe No tremor Joint and vibration sense perfect No ataxia with intended movements, as for instance in the finger—nose or the heel—knee tests Gait unsteady Feet are kept slightly apart when standing and there is a tendency to reel when both feet are kept together closely No aggravation of this reeling with closed eyes The walking movements are slow, staggering, with feet raised unnecessarily high and brought down with a slightly stamping movement

Examination of the blood for Wasserman and Kahn negative

Lumbar puncture—fluid under normal pressure, clear, eight cells (lymphocytes) Albumin and globulin not increased Wassermann—negative

This hereditary disease with symptoms of diplopia, ataxia, exaggerated tendon reflexes without Babinski's sign and the absence of any bony deformity suggested the diagnosis of heredo-cerebellar ataxia (Marie)

In 1935, the patient consulted specialists in Vienna who confirmed the findings and the diagnosis

The patient was seen and thoroughly examined once a year and his condition did not show any material change till 1939 At that time, one intramuscular injection of vitamin B<sub>1</sub> caused an abscess necessitating a break in the routine treatment (exercise and massage) as well as rest in bed for sometime Thereafter, the unsteadiness of his gait had slightly increased without any change of the physical findings, but the use of a stick when walking became necessary

The physical findings remained essentially the same, but since about one year the patient now requires support by another person when walking and the dysarthria also appears more marked Of physical signs, the tendon reflexes are more highly exaggerated and there is adiadochokinesis with quickly alternating pronations and supinations of the fore-arm

The family history of the patient was thoroughly investigated and it revealed 16 cases (11 males and 5 females) of cerebellar ataxia in 5 generations (The 6th generation consists of children and it is too early to judge whether any of them may be affected)

The family tree could be traced to the great-great-grandfather who died at the age of 75 without having been ill himself No data could be obtained about his wife, the great-great-grandmother of our patient and her ancestors, but it can be presumed that through her the disease originated in the family One of her sons, the great-grandfather, is reported to have had an impediment in his speech He died at the age of 45, from an intercurrent disease possibly before other symptoms developed His brother, the great-grand uncle, was

affected at the age of 40 and died when 60 years old with typical signs of cerebellar disease

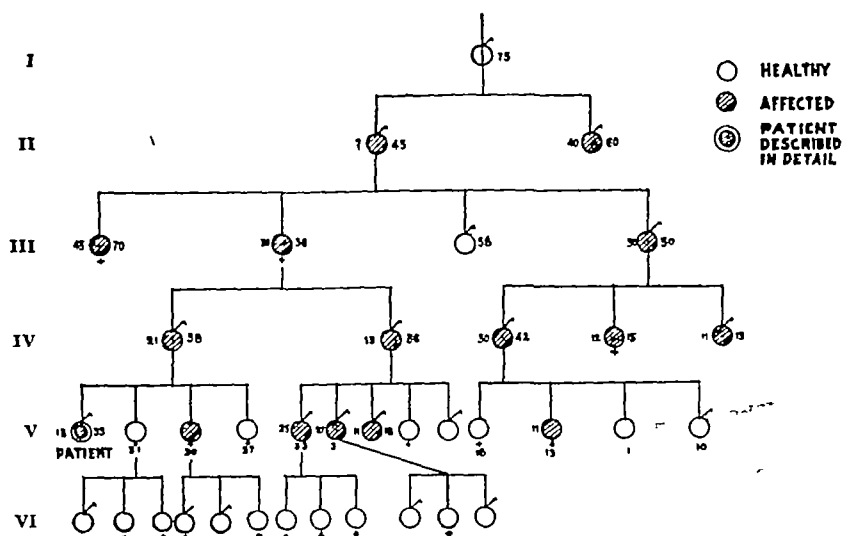


Fig 1 Pedigree illustrating the transmission of Marie's Hereditary Cerebellar Ataxia. The figures for the patient are wrongly printed, 15 should be 25, and 85 should be below the symbol

The distribution of the disease in the progeny will become clear from the family tree where, attached to each symbol the figure on the left represents the age at onset, that on the right the age at death (or the one below the present age)

The disease is inherited as a Mendelian dominant character and the only healthy brother of the grandmother of the patient had six healthy children and seven healthy grandchildren (not incorporated in the family tree)

All the affected members of the family conform closely to the symptomatology of the patient described in detail above and no other cerebro-spinal diseases occurred in this family

This seems to bear out those authors who consider heredo-cerebellar ataxia as a disease entity of its own with pathological changes confined to the cerebellum and without relation to other forms of hereditary cerebrosplinal diseases

The so-called anticipation, meaning the commencement of the disease at an earlier age in successive generations, is quite noticeable in this instance where the average age at the appearance of signs was 42 in the second generation, 32 in the third generation, 18 in the fourth generation but again a little higher (19) in the fifth generation

#### SUMMARY

- (1) A case of heredo-cerebellar ataxia is described
- (2) The family tree shows 16 members so affected
- (3) The heredity is direct and Mendelian dominant

Note.—The complete bibliography can be found in S. A. Kinnier Wilson's *Neurology* Edward Arnold & Co., London, 1940. No relative publications after this date have come to my notice

# Society Proceedings

The 38th Scientific Meeting of the G S Medical College Staff Society, Bombay, was held on Saturday the 10th June 1944 at 9-15 p m (ST) in the Main Lecture Theatre of the College Prof R G Dhayagude was in the chair Dr N M. Purandare read a paper on **RECENT TRENDS IN THE STUDY OF CI WELCHII INFECTION**

After outlining the development of knowledge of anaerobes and giving the incidence of gas-gangrene in pre-antiseptic days, in the last war and present war, the speaker said "Samples received from 210 cases, using various sources such as deep portions of road-side-wounds of patients attending the casualty department of K E M Hospital, cases of tetanus, from wounds in surgical wards as well from post-mortem cases where an infection by anaerobes was suspected, were studied From these 87 strains of pathogenic anaerobes were isolated and identified after studying their morphological, cultural biochemical characters and animal pathogenicity It was interesting to note that from 50 cases of road side injuries studied, no pathogenic anaerobic organism was isolated So also 15 samples of manure and road side dust gave negative results Amongst these 210 samples there was material received from 25 cases of gas-gangrene The grouping of these cases according to the nature of injury was as follows —

Crushed wounds or compound fractures	14
Anaerobic infection secondary to existing gangrene of other type or ulceration	7
Brought about by traumatic peritonitis and intestinal perforation	2
Brought about by nail or needle prick	2
Post natal infection	2
Not known	2
Total	25

The incidence of organisms responsible for these 25 cases of gas-gangrene was as follows —

Ci welchii	10 cases
Ci welchii with Ci septicum	3 cases
Ci septicum alone	6 cases
Ci histolyticum alone	4 cases
No organisms	2 cases
Total	25 cases

Ci Sporogenes was associated with these organisms in 20 cases Two strains of Ci tetani were isolated from the material received from two cases—one of them a case of compound fracture of tibia and ribula developed tetanus two months afterwards Having found that Ci welchii took a major part in causing gas-gangrene, it was studied in detail In order to find the difference between the strains of Ci welchii isolated from cases of gas-gangrene and those from excreta, six-strains of Ci welchii were isolated from samples of human and guinea pig stools (4 from human stools and 2 from guinea pigs) All these 19 strains of Ci welchii varied in their pathogenicity as shown by lethal dose necessary to kill a test animal (white mouse) within a

time A strain of *Cl welchii* S.R. 12, a standard toxigenic strain was brought from Haffkine Institute for using as control strain

Filtrates were obtained from these strains of *Cl welchii* from their growths in media, recommended for toxic production These were then injected in white mice intravenously to note the toxicity It was noted that filtrates from only two strains of *Cl welchii* showed its lethal effect on mice in doses of 0.4-0.5 c.c. The remaining 17 filtrates of other strains failed to show lethal action Filtrate of control strain S.R. 12 killed mice when 0.2 c.c. was injected intravenously

These filtrates were also tested for egg-yolk reaction in order to note their lecithinase activity The principle of this test was that filtrates of *Cl welchii* contained lecithinase which decomposed lecithin of egg-yolk-saline emulsion giving a marked turbidity in the tubes with ultimate creaming of fat According to the degree of turbidity developed and the time taken for this to occur these strains and their filtrates were grouped for their lecithinase activity as follows —

- I Very marked lecithinase activity, of the filtrate of one strain (control strain S.R. 12)
- II Marked lecithinase activity of the filtrates of 2 strains
- III Moderate lecithinase activity of filtrates of 18 strains
- IV Weak lecithinase activity of filtrates of 4 strains

The two filtrates which showed marked lecithinase activity also showed the lethal effect on test animals The same was true of the control strains S.R. 12

Haemolytic activity of these filtrates of *Cl welchii* was studied by using 6 per cent suspension of washed sheep cells Tests were carried out both in normal saline and phosphated buffer solution, the latter showing haemolysis brought about of  $\phi$  factor only All the filtrates excepting one, showed good haemolytic activity

Hyaluronidase content of these filtrates was tested by means of mucin-clot prevention test 17 filtrates showed the presence of this enzyme and in the remaining 3 results were doubtful Maclean and Roger's work resulted in close association of this enzyme with spreading factor produced by invasive micro-organism

From this study it was noted that these strains of *Cl welchii* varied in their pathogenicity Filtrates of two strains and those of control strain showed lethal effect and also marked lecithinase activity showing thereby the predominance of the  $\alpha$  factor in them However in the case of remaining strains, though cultures of these killed mice their filtrates failed to do so, it was possible that, hyaluronidase, a spreading factor was responsible for their pathogenicity The study of the enzymes produced by *Cl welchii* was important particularly from the point of view of early diagnosis of gas-gangrene By simple chemical tests their presence in the oedema fluid of wounds could be made out in a very short time thus giving valuable aid to clinicians

#### DISCUSSION

Dr R. N. Cooper wanted to know what had happened to the two cases of gas-gangrene where no organisms were isolated He also wanted the results of the cultures of cat gut

**Dr A V Baliga** was happy to learn that cultures of road-side dust in the vicinity of the hospital yielded negative results. He asked whether deep X-ray therapy would be beneficial—against the manifold enzyme activities of *Cl welchii*.

**Dr A E DeSa** questioned whether, in view of the fact that these organisms produce a spreading factor, an amputation at a higher level is a more radical procedure.

In reply **Dr N M Purandare** said that out of the two cases of gas-gangrene where no organisms were isolated, one case expired and in the other the ultimate results could not be traced. He suggested that a more radical operation is likely to give better results.

**Prof R G Dhayagude** in winding up the proceedings stated that the samples of cat gut which were studied were received from sealed tubes and not from wounds. He observed that it would be interesting to study the enzymes acting along with the clinical manifestation of the disease. The action of deep X-ray on these organisms, as far as he knew, had not been studied in detail.



## *Critical Notes and Abstracts*

**ANAPHYLACTIC SHOCK AFTER POSTERIOR PITUITARY EXTRACT INJECTION** Schleyer, E (Brit MJ I 225 Feb 19, 1944) A woman, under treatment for menorrhagia, improved with treatment by progestoral (anhydro-hydroxy-progesterone) and intrav 10 per cent calcium injections, but after a severe haemorrhage, a mixed injection of 1cc pituitary posterior lobe ext (glandutrin) and 1 cc neofemergen (ergotamine and ergonovine tartrates) was given intramuscularly. Pain in the head, blurred vision, dyspnea, and swelling of the features followed. Pulse was 140, the skin was red and hot, pain in the stomach and intestines appeared, with vomiting. Two cc coramine (N N-diethylnicotinamide) was given hypodermically, and much frothy fluid was vomited. Breathing became easier. The symptoms, except itching of the feet, the swollen eyelids, and head pains, cleared within 5 hours. A slight irritant rash recurred at the site of injection one week later. A history of urticaria after eating fish in childhood was revealed. No decision was reached as to whether the severe reaction was due to pituitary ext or to the neofemergen, but the former is considered most probable.

**PITRESSIN WATER TEST IN THE DIAGNOSIS OF EPILEPSY, WITH A NOTE ON A FATAL CASE** Immig, W Allg Zeitschr Psychiat 121 216, Jan 25, 1943, Thru Bull War Med 4 40 (Sept 1943) The German literature is generally in favour of the pitressin water test for the diagnosis of epilepsy, but even if properly administered the test can be fatal. One man with a history of fits but no physical abnormalities received 2 injections of pitressin in 4 hours and 1 L of water. During the 10 hours following the 2nd injection he had 10 fits, then died suddenly. Autopsy showed cerebral and pulmonary edema and dilatation of the heart. Administration of a sedative such as Luminal and of 40 per cent hexamine solution, intravenous, is suggested as therapy.

**WATER-PITRESSIN TEST IN THE DIAGNOSIS OF EPILEPSY** (Garland, Hugh G, Dick, A Peter, and Whitty, C W M Lancet 245 566, Nov 6, 1943) As a diagnostic test of epilepsy the patient was kept in bed and was given 1 pint of water every hour from 7 a.m. until the test was discontinued. Doses of pituitrin which, like pitressin, contain vasopressin, were given hourly from 10 a.m. beginning with 0.2 cc, then 0.3 cc, 0.4 cc, and 5 doses of 0.5 cc each, the dose varying with the general condition of the patient and the histamine content and potency of the pituitary prep. Large amounts of fluid are given orally. If a fit occurred, treatment was discontinued and 1 gr phenobarbitone was given orally. Of 44 subjects known to have epilepsy, 19 had fits 5-24 hours after the onset of the test. Five had 2 fits, one 4, and one 5, in one patient vomiting was frequent and rendered phenobarbitone ineffective when administered orally, phenobarbitone for intramuscular injection was not available. Other reac-

tions included pallor, headache, abdominal fullness, nausea, occasionally colic diarrhoea on the following day, etc. None of the controls with hysterical personalities developed fits, but 12 of 32 subjects classed as 'doubtful' developed epileptic fits. No person developed a fit who did not have a history of epilepsy. The test is recommended for use by the Armed Forces in rapid diagnosis of epilepsy in young and otherwise healthy subjects, provided the subjects are kept under constant observation.

**AGE INCIDENCE AND PROGNOSIS OF EPILEPSY** Nattrass, F. J. (Brit. Med. J. II 481 Oct 16, 1943). In 602 cases of epilepsy attacks commenced after the age of 40 in 81 patients. A careful follow-up of these for 12-18 years showed the seizures were not due to cerebral tumors, severe cerebral arteriosclerosis, general paralysis of the insane, or other progressive disease. Idiopathic epilepsy is not uncommon in mature persons, and although fits are indicative of intracranial tumors in some instances, such seizures would not precede all other symptoms by months and years. It was demonstrated that after maturity epilepsy has no marked effect on general health or intellectual powers. No unknown causative factor of the disease was established. Medical students should regard the fits as merely the symptom of an unrecognized condition and continue to search for the etiologic agent in each case.

**THE RAW FOOD DIET A THERAPEUTIC AGENT** Holbrook, Arthur A. (Ann. Internal Med. 20 512-526, Mar 1944). A raw food diet, being low in sodium and high in potassium, is of therapeutic value in various diseases in which sodium chloride and water are retained. Case reports illustrate use of the diet in subacute nephritis, chronic nephritis without edema, thrombophlebitis and inflammatory disease of the liver. The diet was given also to patients with active rheumatic fever, subacute bacterial endocarditis, nephrosis, pneumonia, and catarrhal jaundice. The foods permitted include saltless white bread, orange juice, eggs, saltless butter, jelly, honey, orange marmalade, sugar, celery hearts, carrot, tomato, cucumber, lettuce, mayonnaise, fresh strawberries, grapefruit, fresh pineapple, and shelled almonds.

**MEDICAL MANAGEMENT OF EXOPHTHALMIC GOITER.** Israel, Bram (Philadelphia) (Med. Record 166 345-349, June 1943) discusses the principles that have guided him in the management of patients with exophthalmic goiter, emphasizing particularly diet, medication and psychotherapy. He describes how the thyroid swelling, the single symptom too often isolated for exaggerated attention, undergoes eventual involution during the process of properly applied medical treatment and discusses complications which may appear and the measures he uses in combating them. He illustrates his belief in the dispensability—and even the inadvisability—of surgery in this condition with records of end-results in 3,000 cases seen over 30 years, with follow-up of from 5 to 25 years. Active treatment lasted 2-18 months, depending on age, duration and severity of disease, complications and type of co-operation obtainable. The average patient remained ambulatory throughout with varying reactions on

routine until his symptoms were under control. At the end of the follow-up period 2,640 had become normal as far as Graves's disease was concerned, and the other 360 presented mild, non-disabling sequelae. Four per cent with residual proptosis had had progressive exophthalmos when first seen, and most patients with residua had undergone previous thyroidectomy or extensive irradiation by other hands. Some degree of cardiac enlargement, mainly objective, remained in 35 per cent and mild exophthalmos and heart enlargement in 12 per cent. Clinical mild hypothyroidism remained in 1.2 per cent, who were nevertheless subjectively in good health. The most difficult patients to manage are those (18 per cent in the present series) with a combination of post-operative hypothyroidism and Graves's residua, in whom thyroid replacement therapy may lead to a flare-up in latent Graves's disease. Bram believes that the literature shows a growing reaction against surgery, which directs attention to a single symptom of a complex syndrome still only imperfectly understood.

**PROSTIGMINE IN THE TREATMENT OF EXOPHTHALMIC GOITER. A REPORT OF FIFTY CASES** Bram, Israel (M Record 157 90-92, 109, Feb 1944). Prostigmine (neostigmine) bromide, orally, in doses of 7.5-15 mg t i d for 10 weeks followed by gradual withdrawal of the drug, was given to 50 patients with exophthalmic goiter in addition to general treatment consisting of a 10-hour stay in bed daily, a high caloric diet, etc. Prostigmine seemed to exert an especially favourable influence on the rapid heart rate and exophthalmos, in 28 (56 per cent) patients the basal metabolic rate and pulse were maintained normal for more than 3 years and 14 patients are approaching complete recovery. Of the remaining 8 patients, who are under observation for several months, 6 are progressing favourably, 2 patients with complicating diabetes mellitus are only moderately improved. In exophthalmic goiter, prostigmine combined with quinine is very useful in auricular fibrillation, the combination of 7.5 mg prostigmine, 5 gr quinidine sulfate, and 1/4 gr digitalis ext t i d successfully controlled cardiac excitability and restored rhythm. Prostigmine is contra-indicated in obvious vagotonia, especially with diarrhoea, sialorrhoea, severe sweating, in bronchial asthma, and in marked debility of the aged.

## Book Reviews and Notices

NARCO-ANALYSIS by J Stephen Horsley (pp 134 8s 6d) Oxford University Press, London 1943

This small manual describes in detail the technique of narco-analysis as devised and practised by the author since 1931. The word was coined by him to describe the state of hypnosis produced by a suitable dose of a soluble barbiturate such as sodium soneryl, sodium amytal, sodium pentothal or evipan,—a hypnotic state during which suggestion and analysis are possible. The method is widely used by psychiatrists in mental hospitals as well as in out-patient clinics in ambulatory patients. The intravenous use of soluble, quick-acting barbiturates produces a state of temporarily reduced self-control and self-criticism in which suggestions are readily accepted and in which painful or repressed ideas come readily to consciousness. An artificial contact with the subthalamic or emotional level is readily established and a speedy therapeutic result may be effected. The method is equally useful in diagnosis as well as in treatment of cases of conversion hysteria and states of anxiety neuroses. It is time-saving, safe, and free from the usual disadvantages of hypnosis. The perusal of this manual containing the details of Horsley's technique and the record of his extensive experience, should be indispensable to the physician who intends to use the method in diagnosis or in treatment.

NUTRITION by W R Aykroyd (pp 32 As 6) Oxford University Press, Bombay, 1944

This is No 21 of the useful and topical series, *Oxford Pamphlets on Indian Affairs*, written by well-known authorities on the subjects.

Aykroyd is an acknowledged authority on nutrition in India. He represented India at the United Nations Food Conference, Hot Springs. In a brief survey he has ably summarised the known facts about nutrition in India and once again emphasised that "*the diet of the mass of the population in India is deficient in quality and often in quantity, and much ill-health and disease in India are attributable to malnutrition*". He does not touch the man-made monstrous Bengal Famine of 1943. He deals mainly with the situation as it exists in *normal* times. Apart from the medical aspects of nutrition, diet surveys, dietary deficiencies and effects of malnutrition, he has much to say which is wise, about the population problem, agriculture, food production, and economic aspects of the problem. Though the prospects are gloomy, and the task astronomic in its magnitude, Aykroyd bids us to avoid facile optimism or hopeless pessimism. An attitude of defeatism is not conducive of bold planning for the future. Everyone interested in India should read this pamphlet and remember that *in India the problem is not so much 'right kind of food' as 'enough food.'*

**GOLD THERAPY IN TUBERCULOSIS** by C Dwarkanath, L.I.M (Madras), & Z.T (Hamburg), with a foreword by Capt G Srinivass Murti, the former Principal of the Govt School of Indian Medicine, (pp 61 with many plates and graphs, Rs 2-8-0) published by the author, Nut-shell, Kilpauk, Madras, 1943

The title of the book is rather misleading as the book does not deal with the subject of gold-therapy of tuberculosis, but with the treatment of tuberculosis with an "ayurvedic" gold preparation (a bhasma) administered orally and named *Calci aurum* by the author. The first 2 chapters, more or less, entirely consist of abstracts exclusively from works by Western authors to show that predisposition is far more important than the infection with tubercle bacilli. Chapt III merely contains the views of the classical ayurvedic authors on the properties and effects of gold. No attempt is made by the author to correlate these with the modern conceptions except perhaps to confirm the facts already stated that soil predisposition is of primary importance while bacteria are of secondary importance (rather a dangerous proposition, particularly from the preventive point of view) and that gold hardens the soil. The removal of this chapter from the book will not, at all, break the continuity of the book. Chapt. IV again extensively quotes Western authors on the distribution and mode of action of gold preparations employed in "Western medicine," by injection, with their conclusion that their effect is not parasitotropic but "nosotropic," from stimulation of the reticulo-endothelial system and general bodily defences. All this covers 28 pages while the remaining pages are devoted to *Calci aurum*. Chapt V describes its chemistry and pharmacology from the "Western" point of view. This work appears to have been carried out under the guidance of the heads of the various university departments at Hamburg, but the curious fact is that the names of these authorities are not associated with the publication of the important results, which show that the gold contained in the preparation is absorbed after its oral administration, that it produces no undesirable effects, but on the contrary increases the appetite and weight of the animals and humans treated with it. (In this connection vide Chopra etc Ind J med Res vol xxiv, 1937) Why were these results not published in Germany? There is no reference to any such publication in the book. Did the heads of the Institutes or clinics where they were obtained, consider the data insufficient, or were they not convinced of the beneficial effects? There is no answer to such questions. Finally, Chapt VI is devoted to the clinical results obtained from its use in 22 cases, of whom 2 died, 7 left the hospital before the course of treatment was completed, Case histories of 9 cases are given in the book, while the remaining cases are not accounted for. The number of cases treated and cured is small, and there are no controls. Hence, no conclusions as to the effectiveness or otherwise of the remedy can be drawn.

A.S.P

# Reflections and Aphorisms

## 1 the chronic abdomen

"Our surgical colleagues describe a condition which they speak of, in their clinical slang as the "acute abdomen" There is, however, another condition more familiar to the physician which may be designated with equal propriety the "chronic abdomen," and if the one is, as we are told, a catastrophe, the other is certainly a conundrum

The subject of the chronic abdomen is usually a woman, generally a spinster, or, if married, childless and belonging to the "comfortable" classes To such a degree, moreover, do her abdominal troubles colour her life and personality that we may conveniently speak of her as an "abdominal woman" An abdominal man, on the other hand, is by comparison a rare bird, and when caught has a way of turning out to be a Jew or a doctor The symptoms of the chronic abdomen are many, various, and ever-renewed Some of them refer directly to the abdominal organs, others are of a more remote and general character, but, whatever they are, they are always described with great prolixity and in minute detail Amongst those most commonly complained of are abdominal aches and pains of various sorts and in various places, but especially in the right iliac fossa Instead of actual pain the patient may speak of a "raw feeling inside," or of "an indescribable sensation in the stomach," or of a "dragging" Constipation of greater or less degree almost always figures prominently in the list of symptoms, and flatulence is also frequent Amongst the commoner remote symptoms one finds a feeling of general weakness or "exhaustion" (especially after an action of the bowels), "mental and physical torpor," "inability to think," "a poisoned feeling," and "neuralgic pains all over" Headache and insomnia are also very frequent, and a great many patients complain of undue susceptibility to cold and of a constant catarrh in the throat It will be observed that the road to chronic abdominalism is paved with operations But between the mere dramatic entries and exits of the surgeon, the physician has not been idle The patient has been thoroughly "investigated"—possibly, if she can afford it, at a "teamwork" clinic, she has certainly been provided with an x-ray picture book of her entire alimentary canal, her teeth have been extracted and her tonsils excised, her motions have been analysed by a biochemist and her mind by a psycho-analyst, she has had several rest cures, she has been given prolonged courses of vaccines, of intramuscular tonic injections, of intestinal antiseptics, and of endocrines, she has been fed on sour milk or minced beef or raw vegetables, she has experienced various forms of massage, has been subjected to the latest kinds of electrical current, and has had her colon repeatedly washed out

In a word, she has run the whole gamut of "modern" therapy, has submitted to every "stunt" and conformed to every fad—but is not any better And just as she can only escape the attentions of the doctor when he is "grouse-shooting or salmon-catching or leading his flock in the Upper Engadine," so she is only at peace from the doctor's

the latter is recruiting his exhausted energies by a short holiday in a boarding-house at one of the less expensive seaside resorts

On examination of a fully developed case of the chronic abdomen one will find that it has both a physical and a mental aspect, and that the latter is often the more important of the two

Physically the patient is under-nourished and sallow. To use an abominable term current at the moment, she looks "toxic." The abdomen is of visceroptotic shape and the surface criss-crossed with scars, the signs-manual of the surgeons who at one time or another have conducted exploring expeditions into the interior. The stomach is dropped and splashy and the right kidney more or less movable, there is tenderness at various points over the colon. Constipation will probably be obstinate, and the motions usually show the presence of mucus or even membranes.

The mental side of the case is more difficult to analyse. There is notable, in the first place, a general discontent, "disgruntlement," and peevishness, added to which is an intense egotism which leads the patient to regard herself and her symptoms as of the utmost importance. Needless to say, the patient is intensely introspective and hypochondriacal. She studies and catalogues her symptoms with minute care, and is expert in a knowledge of the action of drugs and a connoisseur of doctors and "specialists."

The operation habit has often a strong hold on her. Added to all this, and most trying of all, is an intense craving for sympathy which must be satisfied at all costs, and it is noteworthy that there is usually some one in her entourage who is always ready to supply the need. Her incessant demand for sympathy and understanding makes the abdominal woman a veritable vampire, sucking the vitality of all who come near her. Half an hour with her reduces her doctor to the consistence of "a piece of chewed string," and is more exhausting to him than all the rest of his daily visits put together, for she is always discovering fresh symptoms, will not admit any improvement in her condition, and has an objection to everything that is proposed. Crabble must have had her in mind when he wrote of the patients—

"Who with sad prayers the weary doctor tease

To name the nameless, ever new disease"

When one comes, then, to analyse a case of the chronic abdomen, it is found to consist on the physical side of a state of visceroptosis along, usually, with a greater or less degree of muco-membranous colitis, (or spastic colon, or gall-bladder dyskinesia) and, on the mental side, of that morbid psychological state which is sketched above. But now comes the conundrum. How can the physical basis produce the multiform symptoms of which the patient complains, and what is its relation to the mental side of the picture?

There remains, when all is said and done, a good deal of mystery about the chronic abdomen, and it needs further study—especially, perhaps, from the psychological side and from the standpoint of the relation of the vegetative nervous system to the emotions."

ROBERT HUTCHISON

# The Indian Physician

VOL III NO 9

SEPTEMBER 1944

WHOLE NO 33

## Original Contributions

### ORGANIC MERCURIALS

THEIR BACTERICIDAL AND FUNGICIDAL ACTION, WITH SPECIAL  
REFERENCE TO THE DERMATOMYCOSES

by

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M D, M R C P, Major R A M C, Medical Specialist to an I G H (C)

WITH THE ASSISTANCE OF

CPL J H CROXON

R. A. M. C.

It has been stated recently<sup>1</sup> that the ideal antiseptic should possess high germicidal and inhibitory properties over the widest possible range of the commoner pathogenic organisms, low tissue toxicity, efficiency in the presence of organic matter, power to penetrate, stability and moderate cost

In this country the commoner pathogenic organisms include a great number of mycotic agents, these latter being especially common in moist, humid regions and during the monsoon period. It is, therefore, considered that the ideal antiseptic should possess a well-marked fungicidal as well as a bactericidal effect. This report intends to show that certain organic mercurial drugs possess the above-mentioned properties in the highest degree and it is felt that, in the latest spate of literature concerning modern antiseptics, this remarkable series of compounds has been greatly neglected.

Before describing the uses and method of application of the above-mentioned drugs, it would be well to explain the rationale governing the use of antiseptics and bactericidal substances whose active agent is a phenol radicle or an Hg cation.

As long ago as 1881 Koch<sup>2</sup> drew attention to the toxic action of Hg on bacteria and Paul and Prall<sup>3</sup> showed that this effect depends on the free concentration of Hg ions in solution.

That this Hg cation was the most effective of the heavy metal cations was proved by Woodroff and Bunzel<sup>4</sup> and later by Winslow and Hotchkiss<sup>5</sup>. This toxic action on bacteria was well manifested in vitro, but it has been shown that in vivo, its bactericidal action is greatly diminished, especially in the presence of organic matter. Chick and Martin<sup>6</sup> consider that this is due to the fact that these cations combine with protein to form an insoluble albuminate, hence the concentration of free ions is greatly diminished, and Clark<sup>7</sup> reported that when a 3 per cent suspension of dried human faeces is added to a solu-



tion of an Hg salt effective in vitro, its activity is reduced by 80—85 per cent. The activity of certain organic mercurial salts under these conditions, is only reduced by 15—20 per cent, and that of phenol is reduced only by 10 per cent. It follows, therefore, that in the presence of organic matter, these organic mercurial salts possess a far greater bactericidal effect than those of the inorganic series, while at the same time, the phenol co-efficient in the former is far greater than that of the latter. The advantage of using these organic mercurials in tissue lesions due to infection is thus clearly established, for it appears that the formation of an insoluble albuminate does not obtain to any marked degree using drugs of this group.

It is proposed to show that the type of organic mercurial employed exerts a significant effect on account of its chemical constitution. The simple aliphatic compounds of Hg have proved extremely toxic in their effect on the human organism. These compounds are represented by the series  $\text{Hg}(\text{R})_2$  where R represents one of the lower hydrocarbon radicles. Mercury dimethyl  $\text{Hg}(\text{CH}_3)_2$  and mercury diethyl  $\text{Hg}(\text{C}_2\text{H}_5)_2$  the most elementary compounds in the series, have a special affinity for the central nervous system, causing rapid degenerative lesions in cerebral and cerebellar areas. The latter compound is, indeed, one of the most interesting in human toxicology, for there is a latent symptomless period of about 16 days between its application or ingestion and the development of C.N.S. signs and symptoms.

The higher compounds of the series of organic mercurials, (aromatic aryl or tolyl compounds) mainly phenyl mercuric acetate, phenyl mercuric chloride and phenyl mercuric nitrate, have been chiefly investigated in the U.S., but Biskind<sup>8</sup> has given a detailed account and reviewed the literature concerning them in an article in the *Lancet* some years ago. (For convenience the above-mentioned compounds will be referred to as P.M.A., P.M.C., and P.M.N. henceforth in this report.)

The bactericidal and bacteriostatic action of P.M.C. was fully investigated by U.S. workers in 1933 and 1934<sup>9</sup>. It was found that the concentration necessary to inhibit the growth of *S. haemolyticus* and *S. aureus* in culture was 1/150,000,000 and 1/125,000,000 respectively.

In England so far, the above-mentioned compounds have been used chiefly in plant chemistry, and the fungicidal action of P.M.C. was investigated in England by Fitzgibbon<sup>10</sup>, using various types of plant fungi. It was shown that this substance is one of the most powerful fungicides known and acts rapidly and effectively in extremely high dilutions.

Byrne and Fitzgibbon,<sup>11</sup> using 0.2 per cent P.M.C. on both H.E.B. and diglycol stearate showed that it also exerts a rapid and specific effect on fungi and bacteria pathogenic to man.

In choosing this particular member of the organic mercurial series, the rationale was as follows:

(1) It was known<sup>12</sup> that the compound  $\text{C}_6\text{H}_5\text{HgCl}$  had a very high bactericidal potency, with a relatively low local and systemic-toxicity for animals and for man.

(2) This effect is due to the action of the compound  $C_6H_5Hg$  ion, and it is thought on theoretical grounds that the bactericidal power of Hg is greatly increased by using it in the form of a phenol derivative

Experiments by Reichel<sup>13</sup> on the dispersion phases of phenol between oil and water suggested that the action of phenol is not so much chemical as physical, the phenol being capable of passing into solution in such substances as coagulated albumin, certain lipoids and the cytoplasm of bacteria. He suggested, therefore, that its action results from its penetration into the bacterial cell in the form of a colloidal solution. Moreover, in the presence of serum, no diminution of the germicidal action of phenol occurs<sup>14</sup>

(3) Though the solubility of P M C is extremely low, this does not detract from its effectiveness. The active portion is the  $C_6H_5Hg$  ion and it is considered that this radicle enters into some form of colloidal solution in the cytoplasm of the infecting fungi or bacteria, and hence a continual removal of  $C_6H_5Hg$  ions takes place from the vehicle or filler in or on which the drug is presented to the infecting organisms. There appears to be something in the nature of a continual bombardment of the organisms with organically combined Hg. It is considered on theoretical grounds that its effect is to cause a rapid disturbance of metabolic function leading to the death of the infecting agents.

P M A has also been used in the investigation, but as this compound has a marked affinity for Cl, the change from P M A to P M C takes place immediately on contact with NaCl, and this latter salt being an invariable constituent of tissue fluid, it was felt that the direct application of the ultimate chemical product should be made. This report, therefore, deals mainly with the action of phenyl mercuric chloride.

As in all bactericides the reaction velocity of P M C depends on its concentration in the area in which it is to exert its action, but owing to its tendency to produce a vesicant effect on tissue or skin, the concentration used must be carefully limited. If a 1% concentration is applied for some hours to skin lesions caused by bacteria or mycotic agents, an extremely rapid bactericidal and fungicidal effect is obtained, but the surrounding healthy skin areas become erythematous or vesicated and do not recover for a further 48-72 hours. In practice, it has been found that 0.25% P M C or 0.25% P M A represent the maximum that can be used without producing these effects. 0.5% P M C adsorbed on a calamine filler, can be used on moist skin lesions without side effects, as the physico-chemical mechanisms obtaining when the drug is presented in this way, are entirely different from those which occur when emulsifying or aqueous vehicles are used.

This latter method (adsorption of a practically insoluble compound on a filler) is thought to mark a new advance in the presentation of a substance (which is almost insoluble in ordinary media) to the infecting agents on which it is to act.

An alternative method is the preparation of a colloidal solution of the drug, but the grave disadvantage in this method is that, in using colloidal solutions of a drug, the bactericidal activity of which is an ionic property, the protective colloid removes the charge from the active cation and hence nullifies its therapeutic effect

#### PHARMACEUTICAL DETAILS OF THE PREPARATION OF P M C AND P M A APPLICATIONS

By H FINE, M P S, Sergeant R.A.M.C

Experimental work on the preparations of P M C and P M A applications presented several temporary difficulties, owing to the conditions under which the work was carried out. Being in an area well forward, facilities for acquiring pharmaceutical elegance were often desired but were in no way forthcoming. Apparatus available was elementary and the only method of registering temperatures was by means of crude, though accurate, improvised thermometers.

It was necessary to consider the physical properties of P M C and P M A very carefully in order that their incorporation into suitable bases would satisfy the following requirements —

(a) To possess the necessary pharmacological and bactericidal action

(b) The preparations to be easily made in Field dispensaries using the least amount of dispensing apparatus

(c) The final products to be stable, capable of being easily applied, and able to be used in all the various areas in which the infecting agent was present

Arising out of the third point, it was decided that, for moist infected areas, a drying lotion would be necessary, and for dry infected areas, an emollient (using an emulsifying base) would suit the case.

Accordingly, P M C and P M A were incorporated in 3 types of base

- (A) In a Eucerin an distilled water base
- (B) In an adhesive lotion of the lotio calamine type
- (C) In simple solution in distilled water

#### (A) Eucerin and distilled water base

P M A is soluble in hot distilled water up to a concentration of 1.5%. P M C is practically insoluble in water. It was found that 2 methods were necessary in order to incorporate P M A and P M C in this emulsifying base

#### (a) Phenyl mercuric acetate (P M A)

P M A.	0.125%
Eucerin	3 parts
Distilled water	5 parts

The P M A is dissolved in distilled water heated to 85°C. This solution, while still warm, is slowly added to the Eucerin previously melted and kept at a temperature not exceeding 55°C. The mixture is continuously stirred until cool, when a white homogeneous cream is produced, which is easily absorbed into the skin with the minimum of friction.

## (b) Phenyl mercuric chloride (P M C)

P M C	0 20%
Eucerin	3 parts
Distilled water	5 parts

As P M C is practically insoluble in water, the most efficient method is to incorporate the P M C with the melted Eucerin at 55°C, using careful trituration and keeping the contents of the mortar heated to 55°C by means of a water bath. It is essential that the P M C be as evenly dispersed as possible in the melted Eucerin before adding the distilled water (heated to 85°C) in small quantities, with constant stirring. The whole is now allowed to cool rapidly, stirring until a white homogeneous cream is obtained. This product, too, is quite easily emulsified into the skin.

Even more perfect diffusion of the active constituent could be obtained if the final product could be put through a homogeniser of the "Empire" hand type. Unfortunately, owing to the limited apparatus available, this could not be done in this dispensary.

(B) *Adhesive lotion base*

For moist surface infections it was decided to use local treatment to the affected areas by means of a lotion which possessed the following properties

(1) Sufficient concentration to exert the maximum bactericidal action

(2) To enable the area to be gradually dried

(3) To prevent any aggravation of irritation and, if possible have the maximum cooling effect

(4) To remain in contact with the area for a prolonged period, although the area may be constantly moist, due to perspiration

(5) To be easily applied

All these conditions were satisfied in the product of the following formula

P M C 0.5% impregnated on calamine	B P	gr	XV	(15)
Zinc oxide		gr	XXX	(30)
Glycerine		m	XXX	(30)
Aquam ad		oz	1	

A supply of calamine impregnated with 0.5% P M C was supplied by the courtesy of Lunevale Products Laboratories, U K

Probably, owing to the method of preparation, the impregnated calamine was found to be very much more "dense" than Calamine B P, and thus required a large amount of zinc oxide and glycerine to maintain an even suspension when shaken, and sufficient adhesiveness when applied to the infected area. The method of preparation is identical with that of lotio calamine, although it must be stressed that the two insoluble powders be very carefully mixed and sifted before adding the glycerine and required amount of water.

(C) *Solution with distilled water*

For large infected areas of deep seated origin, and for open infections of the "jungle sore" type, it was found that an application of a solution of P M A had the desired therapeutic effect

Varied concentrations were tried and the following solution found to be the most satisfactory —

Phenyl mercuric acetate	0.05%
Sterile distilled water	oz 1

Solution is effected by heating up 2 grams of P.M.A. in 250 cc of distilled water and pouring the almost boiling solution into 750 cc cold distilled water. Stir well and allow to settle. Filter from sediment of which there will be traces. This stock solution can be regarded as 0.2% W/W or W/V for all practical purposes. The desired strength of solution may then be obtained by further dilution with the required amount of cold distilled water.

Owing to the extraordinarily high phenol co-efficient of P.M.A., conditions for making this solution do not necessitate the use of rigid aseptic precautions as even in this dilution it is found that the solution is itself self-sterilising.

A survey of the above methods of preparing P.M.A. and P.M.C. applications shows that it is within the scope of any dispensary in the field to dispense these preparations. They are easily and quickly made, and the final products are pharmaceutically quite elegant.

#### METHODS OF APPLICATION OF THE ABOVE PREPARATIONS OF P.M.C. AND P.M.A.

At the commencement of the investigation the cases were treated as follows —

Cases from the Convalescent Wing of the C.C.S. where this work was carried out were treated as out-patients, attending at the M.I. Room twice daily, where thorough inunction of P.M.C. ointment was carried out. Though results were eminently satisfactory it was found that the method was wasteful in the use of the limited amounts of ointments at our disposal, and so all the convalescent cases were admitted for 1-2 days to the Skin Section of the C.C.S., where the ointment was applied on lint and bandaged on to the affected areas.

As the reaction velocity of P.M.C. depends both on the concentration applied and the duration of application, it was found that the latter method mentioned above effected a great saving in the amount of ointment used, and produced a much more rapid curative effect. It was later found that if the method of application outlined below is carefully adhered to, hospitalization of infected patients is quite unnecessary.

The types of mycotic infection observed, affecting the trunk and limbs, varied enormously, presumably due to the nature of the infecting fungus, and the skin reaction of the patient. It is considered that variants occur in the strain of fungi akin to those occurring in bacterial infections in man. Dry, superficial, circinate infections of large extent and rapid spread alternated with those producing agminate folliculitis, and maculo-papular lesions of both guttate and punctate varieties were found. Epidermophyton infections, i.e. *E. inguinalis* and the so-called "foot-rot" are among the commonest lesions met with. As stated above, the type of application varied

with the nature of the lesion and in general the following principles of treatment were adopted —

- (1) *Agminate Folliculitis* One application of 0.20% P.M.C. was used on lint, after thorough cleansing of the affected part. The ointment was left in contact with the lesion for 3-4 hours after inunction.
- (2) *Dry, spreading, circinate lesions* A four hours' application of 0.20% P.M.C. on lint was carried out, and for the raised maculo-papular type of lesion, this treatment also proved eminently successful.

Occasionally, some small lesions of the guttate type proved resistant to treatment. 0.25% P.M.A. in chloroform applied to these caused a rapid resolution, though in a few cases a temporary vesication was produced. In view of the extreme rapidity of the control of the infection this latter effect (which was quite mild) was not considered to have any detrimental action, and all side effects cleared up in 24-48 hours.

For moist open lesions preliminary treatment with (0.20%) P.M.C. on lint for three hours was used, followed by the P.M.C. lotion (0.5% absorbed on calamine). Clearance of the lesions occurred in 2 or 3 days.

#### 'FOOT ROT' — EPIDERMOPHYTOSIS OF THE FEET

The interdigital spaces were thoroughly cleaned and all dead skin removed. 0.5% P.M.C. on calamine was used in powder form where moist lesions occurred and when area was dry (usually 24 hours after the powder application) 0.20% P.M.C. ointment or 0.125% P.M.A. ointment was used. It is essential to keep a careful check on the state of the lesions and vary powder, lotion or ointment in order to keep the skin in its normal condition.

#### EPIDERMOPHYTON INGUINALE — (DHOBIE ITCH)

This type of infection was treated by one application of 0.20% P.M.C. After thorough inunction into the affected area, paying special attention to the infected spreading edge, strips of lint coated with the ointment were applied to the lesion and fixed in position by means of pads of cotton wool and a double T-bandage. Four hours' application was usually sufficient to cause complete disappearance of the lesion. Regarding epidermophyton infections of the toes, recurrences are mainly due to the following causes —

- (i) fresh infection from an outside source, and
- (ii) re-infection from the socks or the footwear of the patient.

The spores of the causative fungus remain in or on the patient's socks or footwear and are not destroyed in washing (by the usual dhobi method). It is essential to steep the socks overnight in 1/1,000 perchloride of mercury or, better still, 1/2,000 P.M.A. solution to ensure thorough destruction of spores. The socks can then be rinsed and washed in the usual manner. Some spores remain in the boot or shoe and, as treatment in a disinfectant renders these articles unserviceable for further use, it is suggested that thorough treatment with 1/1,000 P.M.A. solution will rapidly render them free from spore contamination.

### 'JUNGLE SORES'

Preliminary local cleansing with removal of all dead organic matter from the affected part was carried out 1/2,000 P M A. compresses were applied for 6 hours, to disinfect the lesions thoroughly Elastoplast was then applied Extremely rapid healing occurred, as both bacterial and mycotic infecting agents had been destroyed and the sores rendered practically aseptic

For open infected wounds of all varieties, application of dressings soaked in 1/2,500 P M A gave rapid and excellent results, the infected area being completely disinfected in 24 hours All dead organic matter must be removed as far as possible before applying this solution

The number of open infected wounds treated was small but results were rapid and spectacular A fuller investigation of the effects of P M A on these conditions is now proceeding, and a report will be published later, when a number of cases sufficient to show results of significant statistical value has been treated

In some of the dermatomycoses recorded above, 0.125% P M A ointment was used The results differed in no way from those effected by P M C The method of application and period of contact employed was the same for both compounds

Following application of the above ointments, slight and temporary vesication may be seen in some cases, especially round the spreading edges of the lesion, but this disappears after 24 to 48 hours, leaving a clean healthy skin beneath Secondary infection does not occur, as the minute vesicated areas remain aseptic in view of the powerful antiseptic action of the compound used

NUMBER OF CASES TREATED	250
Classification	
(i) Ringworm of trunk and limbs	115
(ii) Tinea Cruris ( Dhobie itch )	62
(iii) Epidermophytosis of feet	20
(iv) Jungle sores	32
(v) Infected wounds of various types	21

In groups (i) and (ii) a single application of 0.20% P M C or 0.125% P M A for 3 to 4 hours caused complete healing of the mycotic lesions In group (iii), 2-5 days were sufficient to bring about clearance of the disease In group (iv) after preliminary application of 1/2,000 P M A. disinfection of the lesions occurred and the application of elastoplast gave rapid and satisfactory results In group (v) the small number of cases so far treated have shown extremely promising results, and further investigation in an extended series of cases is now being carried out

As regards group (iii) it was found that when the infection was seen at an early stage, 24-48 hours' treatment with 0.5% P M C powder was sufficient to effect cure Where a superimposed cheilopompholyx is present somewhat slower curative effects are obtained

It must be emphasised that the rapid cure of epidermophytosis of the interdigital spaces is only possible when the lesion is seen at a reasonably early stage Many cases have been seen when this infection has been present for years, in these cases hyperkeratosis and fissures are present, and it is quite impossible to effect permanent

cure by the above methods of treatment, the reason being that while a temporary cure is effected by the destruction of the vegetative form of the fungus, the resistant spores remain below the hyperkeratotic areas. No matter how effective the fungicidal agent used, and how efficient the emulsifying base in which it is presented, the conditions obtaining in the chronically infected areas do not permit of the effective destruction of the spores of the responsible mycotic agent, and relapses are bound to occur.

X-Ray therapy represents the only efficient method that can effect permanent cure in these cases.

As regards the types of application mentioned above, it is essential that the method of application and duration thereof be strictly adhered to in order to effect that rapid cure which has been described.

#### SUMMARY AND CONCLUSIONS

(a) Phenyl mercuric chloride and phenyl mercuric acetate in plant mycology are recognised as possessing specific and rapid fungicidal effects in high dilution.

(b) Similar effects obtain in the case of the fungus infections occurring in man.

(c) The bactericidal potency of these drugs is extraordinarily high, and work is being carried out on their action as surface anti-septics. Preliminary results are extremely satisfactory.

I wish to thank Lt Colonel P D Johnson R.A.M.C. O.C. 9 British C.C.S. (at which unit most of this work was carried out) for permission to publish this report. My thanks are also due to Mr M Fitzgibbon F.I.C. Lunevale Products Laboratories, Lancaster, U.K. for generous supplies of P.M.C. and P.M.A. and for the special calamine preparations referred to and for his helpful suggestions regarding certain technical details. I am also indebted to Sergeant H Fine R.A.M.C. for his work in the preparation of P.M.C. and P.M.A. applications.

This investigation would not have been possible without the painstaking and detailed co-operation of the orderlies in the dermatological section, to whom I must pay a special tribute for their excellent work.

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- 4 WOODRUFF C L and BUNZEL H H (1909) *Amer J Physiol* 25 190
- 5 WINSLOW C E A and HOTCHKISS M (1922) *Proc Socy Exp Biol N.Y.* 19 314
- 6 CHICK H and MARTIN C. J (1908) *J Hyg Camb* 8, 608
- 7 CLARK *Applied Pharmacology* (1940) Churchill, London
- 8 BISKIND L (1935) *Lancet* ii 1049
- 9 WOOD and ECKER (1938) *J Infect Diseases* 52, 354 and 53 350
- 10 FITZGIBBON M. Personal communication (1942)
- 11 BYRNE and FITZGIBBON (1942) *Report to Frankl and Socy*
- 12 BISKIND L (1935) : *Lancet* ii 1049
- 13 REICHEL H (1909) *Biochem Z* 22, 149
- 14 BROWNING et al (1917) *B.M.J* i 73

(Continued from page 296)

goitre was a real one and must always be kept in mind. Goitre was only a symptom, and exaggerated attention should not be paid to it, but the patient's whole personality should be reviewed and the treatment planned accordingly. Dr Patel also stressed the importance of large doses of vitamin A in Graves's disease.

In view of the difficulties regarding the estimation of B.M.R., a plea was made to make use of Basal Temperature as a guide to B.M.R. The temperature was taken in the mouth or in the rectum between 5—6 in the morning before the patient got up. The speaker had found the method useful in detecting masked myxaedema, well as in regulating the dose of thyroid extract in  $\lambda$ -hypothyroid conditions.



# Society Proceedings

The 39th Scientific meeting of the Seth G S Medical College Staff Society was held on Saturday the 15th July, 1944 at 9-15 p m (NST) in the Main Lecture Theatre of the College Dr R N Cooper was in the Chair Dr K G Munsif read a paper on

## SURGERY OF THE THYROID GLAND

Surgery of the thyroid gland has made rapid advances in recent years The number of cases admitted in our Hospital is steadily increasing as you will see from Table I, where an attempt is also made to work out the age incidence You will see that the maximum number of cases are in the 2nd and 3rd decades of life You will also observe from the table that we have had no cases in children It may be that our sister institution across the road, viz the Bai Jerbai Wadia Hospital for Children is taking them before they reach us Out of these 192 cases, 135 cases were operated upon, and of these 17 died The mortality works out about 11 per cent

Table II (all Tables are printed together before discussion) represents the classification and number of cases in each group

### I TOXIC GOITRES

I propose to confine my remarks to cases of toxic goitres and to tumours, as Hashimoto's disease and Riedel's thyroiditis have been discussed here before We have had 53 cases of toxic goitres, out of which 37 have been clinically evaluated as Primary toxic and 16 as Secondary toxic goitres In Table III an attempt is made to show you the age in decades and the duration of symptoms You will notice that while in Primary toxic goitres the duration of symptoms is in months, in Secondary toxic goitres it is in years In my personal series of 24 cases, I have had 3 of Primary toxic and 5 of Secondary toxic goitres

You will agree when I say that no groups of surgical cases offer any greater opportunity for satisfactory and gratifying results both to the patients and their surgeons as do cases of hyperthyroidism I should have liked to give you a separate review of thyrocardiacs but I am sorry to say that the paucity of case notes prevents me from doing so I have therefore put them along with other cases of hyperthyroidism

(1) *Pre-operative Preparation*—The proper pre-operative preparation of a hyperthyroid patient is extremely important As a routine, rest and Lugol's solution are given with sedatives and isolation or restriction of visitors when necessary Here I may quote one of my cases where the presence of the step-son, increased the pulse rate and irritability In thyrocardiacs, it is important to digitalise a patient and in some cases of cardiac failure where oedema persists diuretics are indicated Such cases should always be treated with the co-operation of a physician One word about administration of iodine in thyrotoxicosis, it should not be administered unless proper plans for surgery have been made Iodine-fast patients with hyperthyroidism

are a great surgical risk and one would like the physician to recognise that surgery is a comparatively safe and rapid method of curing hyperthyroidism and that in outspoken thyroid toxicity, iodine does not produce a cure. Electro-cardiogram should be taken as a routine in all thyrocardiacs. X-ray examination is important to note the deviation of the trachea especially in intra-thoracic goitres. Unfortunately we did not have a single case of intra-thoracic goitre in our present series.

For some years now, we take the B.M.R. as a routine in all hyperthyroid cases. Though I have tried to work out the figures in many cases, I shall keep back this table as I do not wish to inflict many tables upon you. I may mention that the highest figure obtained was in one of my cases, viz. +56 Mayo Clinic Standard. This lady after rest, Lugol's solution and isolation came down to +22 and the pulse rate dropped from 120 to 84. Basal metabolic rates when high, are approximate measures of the intensity of the toxic process but are not reliable indices for estimating the degrees of operative risk. It is said that in primary toxic goitre if the B.M.R. comes down after rest, Lugol's and sedatives, it is of a good prognostic significance. While a high rate usually accompanies severe hyperthyroidism, a low rate does not necessarily mean a milder degree of toxicity and certainly is no indication of the patient's ability to withstand the intoxication or operation. One comes across patients with normal or relatively low basal metabolic rates who may even have a pulse rate of 80 to 90 and yet are markedly activated, whose hands are hot and moist and who have lost considerable amount of weight. One must measure the degree of intoxication by many factors and one's judgment as to the degree of risk is often substantiated by the patient's course while undergoing operation. Basal metabolic rates ordinarily are higher in Primary than in Secondary hyperthyroidism. In Dr Cooper's unit, Dr Glinde with his assistant is working on the adrenaline test for toxicity.

The pre-operative preparation takes about two weeks on an average. In serious cases it takes much longer. The technique I have employed is similar to Crile's 'Stealing' the thyroid. A bandage is put round the neck and an enema given every day. On the day of the operation instead of the enema, the patient gets a basal narcotic. One has used avertin when it was available, the dose fixed by the anaesthetist previously. Now paraldehyde is given per rectum. I have also used pentothal intravenously in the wards. The sleeping patient is wheeled to the theatre where under intratracheal anaesthesia the operation is carried on. Formerly I used local infiltration which I have now discontinued.

One word about anaesthesia. This is extremely important in these operations. It is suggested by American authors that a mixture of helium and oxygen should be used, for helium reduces the molecular weight of oxygen and thus the mixture readily diffuses in circulation. It is also mentioned that from the amount of oxygen a patient is consuming on the table, the toxicity can be gauged. It is pointed out

that a moderately toxic patient will require 200 to 400 c.c. of  $O_2$  per minute, whereas the high risk patient will consume 600 to 800 c.c. of  $O_2$  per minute. On the face of these warnings, stage procedures must be employed to avoid fatalities. The rise in pulse rate during the operation—again the work of the anaesthetist—is a warning for stage procedures. I must here mention that in all the cases I have done, I have not had to regret the choice of my anaesthetist.

(2) *Operation Proper*—With the proper pre-operative preparation, in the cases I have done, I have not had to do operation in stages. This does not mean that one can always get away and is not an argument against graded operations. In our series there are three cases where operation has been carried out (successfully in two)—by graded surgery and they have been cases with severe hyperthyroidism. Blood transfusion is given during the operation in the majority of severe toxic cases.

The technique employed is one that is well-known, viz. sub-total thyroidectomy. In very vascular cases, I have tied all the four vessels. I do not, however, ligature the inferior thyroid arteries as a routine. If the posterior wedge is left behind with care, no injury occurs to the parathyroid bodies. In my personal series I have had no cases of tetany following the operation.

One word regarding the incision—The low collar incision is alright in small enlargements, but in big enlargements the incision, in my opinion, should be made over the most convex part. This makes the reflection of flaps and access to the superior poles easy. It is also important to reflect the upper flap well above the notch in the thyroid cartilage, since, if this is not done, it will be impossible to make the lateral elevation above the level of the superior thyroid arteries, so that they can be visualised. The cutting of the pre-thyroid muscles I do now as a routine. I have only very recently learnt that they should be divided high up, not only to preserve their nerve supply but also to ensure a good scar.

The bleeding from the cut thyroid is controlled by previous application of haemostats and the oozing controlled by criss-crossing or by suturing the portion to the side of trachea. I have in majority of cases inserted split drains, though it is recommended by some that no drains are necessary. In the post-operative treatment, I give glucose saline 10 oz. containing 30 min. of Lugol's iodine with chloral hydrate 30 grs. and bromide 15 grs. as a routine. Lugol's solution is continued for at least two weeks in severe cases of hyperthyroidism.

The drains are removed in 24 hours and the clips in 48 hours. Thiourea and thiourecil are recommended in the treatment of hyperthyroid cases. I learn that physicians are trying it out. We are awaiting their results.

## II TUMOURS

(1) *Classification*—In our series we have had 3 cases of foetal adenomata and 20 cases of primary malignant tumours. From the study of these cases Table V is evolved. You will see from this table that in 17 cases out of 23 malignant tumours a histological diagnosis was

obtained. The other six were admitted with the clinical diagnosis of carcinoma thyroid. Out of these, two expired before anything could be done and one discharged against medical advice. Out of the remaining three, in two tracheotomy was done to relieve respiratory obstruction and in one no histological report is available. The histological diagnosis given in this table can best be discussed by the pathologists. I shall therefore leave it to them and especially to Prof R G Dhayagude. As clinicians we like to know the degree of malignancy. From Lahey Clinic comes a classification which I think would be very helpful to us. It is given in Table VI. Such a classification will enable us in future to study the results of our treatment. Out of the 17 cases, 15 were operated upon, in 3 a biopsy was taken. Out of the 15, 2 died. All were advised X-ray therapy.

(2) *Diagnosis*—It is well-known that diagnosis of carcinoma thyroid is not easy in every case. I am demonstrating a case of a lady aged 50 years, who was admitted for a thyroid swelling of a year's duration. She complained of palpitation and weakness of about 15 days' duration. The swelling in the neck was 6" by 4" with a nodule in the lower pole on the left side. Patient had hoarseness of voice. Her pulse rate was 65 and was irregularly irregular. Her blood pressure was 120-75 and B.M.R. was +1. No electro-cardiogram could be taken as the machine was out of order. Dr Vakil was consulted and though he could not say what was the cause of irregularity of the pulse, he said that it was a contra-indication to operation. Clinically I thought that it was a "Thyrocardiac" case. I had suspected no malignancy. On operation table after the thyroid was exposed, the gland felt very firm and it looked relatively a vascular. Sub-total thyroidectomy was done and the report was adeno-carcinoma.

I must here mention that she gave me no trouble during and after operation though I expected it. Her pulse continued to be irregular. She was shown at the surgical consultation meeting where I agreed with my other colleagues that she should be given deep X-rays and watched for the present, and not submit her to a total thyroidectomy. In this case I must mention that the pre-tracheal muscles were not at all adherent to the gland.

(3) *Operation*—In the technique of total thyroidectomy, no attempt is made to separate the pre-tracheal muscles. The sternomastoid with the internal jugular vein on the affected side is sacrificed, together with all the lymph nodes. Even if complete extirpation cannot be effected it is good to remove as much as possible so that roentgen rays may be able to accomplish the rest. Sometimes formidable tumours which appear inoperable have been made operable by previous irradiation. There are cases on record who have lived many years even after a secondary deposit in bones in whom the thyroid has been removed.

### III COMPLICATIONS OF OPERATIONS ON THE THYROID

(1) *Thyroid Crisis*—In the early days (as a Registrar) I had seen thyroid crisis following a partial thyroidectomy in a hyperthyroid case. In my series, I have none. This is possibly due to greater

in pre-operative preparation When it does occur it is a very exaggerated picture of toxicity High temperature, restlessness, even delirium and fast pulse are predominant High temperature is treated by cold sponging, restlessness by morphia and iodine is given to combat toxicity It is recommended that besides Lugol's iodine, 5 grs of sodium iodide should be injected intravenously Oxygen tent in these cases is of great help Glucose saline intravenously in large amounts is given to preserve the fluid balance and digitalis is administered if fibrillation develops (Four cases have been recorded in our series where this complication occurred)

(2) *Injury to the recurrent laryngeal nerve*—Paresis due to stretching does not give much anxiety Complete paralysis gives rise to permanent hoarseness In our series, we have had three cases where this complication occurred

(3) *Injury to the superior laryngeal nerve*—A rare complication which leads to abolition of cough reflex and thus predisposes to chest complications has not been noticed in our series

(4) *Tetany*—This is due to removal of parathyroids or temporary interruption of their functions due to oedema In mild cases, for example, numbness in the arms and slight carpopedal spasms—20 units of parathormone suffices It raises the serum calcium to the normal level in 6 hours and maintains it at that level for 24 hours In our series, we had one mild case which responded to injection of calcium gluconate

(5) *Myxoedema*—Due to excessive removal of the thyroid tissue may develop within a few weeks of operation Prolonged post-operative administration of iodine is thought to predispose to its development at a later stage The treatment is to give thyroid extract

(6) *Collapse of trachea*—This is a complication which should be treated by tracheotomy I feel that failure to do this resulted in three deaths in our series

(7) *Infection of wound*—This has occurred in five cases, I have had one which was due to the linen I used My feeling is that the rest were due to the same cause

#### V CONCLUSION

From the study of these 192 cases, one has realised the importance of proper recording It is a pity as all of us know, that our recording is far from satisfactory From the study of the thyroid cases, special emphasis should be laid on the following points

- 1 What is the first sign or symptom to appear
- 2 Any psychological trauma
- 3 Any treatment taken previously

In the physical examination, the measurements of the swelling in the neck, proper tabulation of the eye signs, of symptoms referred to central nervous system, to the cardio-vascular and the alimentary system, loss of weight if any, and pressure phenomena should be recorded.

The investigations should be properly tabulated For such a thing, I suggest that a scheme be drawn out by all the surgeons and it be

followed by all the units I am sure that after another ten years, if the above is carried out, we shall have something in thyroid surgery to show, of which we can justly be proud

#### DEMONSTRATION OF CASES

**Case I—Primary Toxic Goutre** Female, age 30 was admitted in this hospital for a thyroid swelling of six months' duration. Two months after the appearance of the swelling she started getting tremors of the hand marked irritability, sleeplessness protrusion of the eye balls and palpitation. Her pulse rate was 102 B.M.R. was +31. Leucocyte count was 12 000 out of which 50 p.c. were lymphocytes. She was getting extra systoles in the wards, but electrocardiogram showed nothing abnormal. She was kept on Lugol's iodine 15 minims, three times a day with bromide mixture. After 13 days the pulse rate came down to 84 and the B.M.R. to -6 (?). The tremors disappeared and there was improvement in the exophthalmos. She was operated upon the next day without the patient knowing about it. Paraldehyde drachms seven with ten ounces of saline were administered an hour before the operation. Subtotal thyroidectomy was performed under intra tracheal ether anaesthesia. In this case I have not tied the inferior thyroid arteries. She gave no trouble during the operation. Her pulse rate went up to 90 only.

Lugol with sedatives, as already suggested were given post-operatively. She has done well. There is a marked difference in her exophthalmos.

**Case II—Secondary Toxic Goutre**—Female, age 34 came to the hospital for a thyroid swelling of 12 years duration. For the last five years she noticed that the swelling increased more rapidly than before. Fifteen days prior to admission, she started getting marked palpitations hunger and diarrhoea. There were no eye signs. The swelling in the neck was about 3" x 1" and firm to feel. Her pulse rate was 90 B.M.R. +3. She was operated upon under sodium pentothal in the wards and intratracheal ether in the theatre. The right lobe felt very firm. It was completely removed 3/4th of the left lobe was removed. She made an uneventful recovery.

#### Histological Diagnosis—Involutional Goutre

All her symptoms have disappeared and she feels very much better.

**Case III—Idenoma of Thyroid**—Female age 30, having swelling in the region of the thyroid of 2 years duration was admitted for pain and swelling which increased after delivery since the last 2 months. There were no toxic symptoms. During operation, the pretracheal muscles were found to be markedly adherent to the two nodules in the right lobe of the thyroid gland. They were excised. The section report was colloid adenoma. The case has been demonstrated because of the peculiarity of the adherence of the muscles to the benign adenomata.

**Case IV**—Female aged 50 was admitted for a thyroid swelling of two years duration. About two weeks prior to admission she had difficulty in swallowing both solids and liquids. There was a firm swelling on the right side 2" x 1 1/2", the skin was free and it was not adherent to the deeper structures. Lymphatic nodes in the neck were not enlarged. There were no other toxic symptoms. Laryngoscopy revealed nothing abnormal. B.M.R. was +15. She was suspected to be (?) malignant.

A hemithyroidectomy was done. The recurrent laryngeal nerve was exposed and carefully separated. Section report showed Colloid Adenoma.

TABLE I  
SURGERY OF THE THYROID GLAND

Total number of cases from 1st July 1934 to 30th June 1944—A period of 10 years

		Total No		Operated cases		Operative Mortality
Present series		102		135		17
Own cases		24		20		2
Sex Incidence		Male 73		Female 119		
percentage ratio		38 p c.		62 p c		
		1		16		

Number of cases in each year and their age incidence.

Years	Age in decades						No of cases in each year
1 10	11 20	21 30	31-40	41 50	51 60	61 70	
1934(1)		2	2	3	1	1	9
1935	1	4	1	1			7
1936	1	8	1	1			11
1937	3	8	1	2	1		15
1938	4	6	4	2	1		18
1939	3	4	3	2			12
1940	8	5	8	2	3		26
1941	7	3	3	5			18
1942	6		5	4			15
1943	5	11	10				26
1944(1)	1	3	4	4			12
Total	39	61	42	24	11	2	129

**TABLE II**  
**Classification of the Thyroid Diseases in the present series**

I	Non Toxic Goitres		93	IV	Hashimoto's Disease (2 confirmed microscopically)		3		
	1 Single Nodules	50			V	Riedel's Struma (1 confirmed microscopically)		1	
	2 Multiple Nodules	34				VI	Inflammations		4
	3 Diffuse Enlargement	9					(a) Acute	2	
			98		(b) Chronic	2			
II	Toxic Goitres		53	VII	Thyroglossal cysts		5		
	1 Primary toxic goitres	37			VIII	Thyroglossal fistulae		3	
	2 Secondary toxic goitres	10				IX	Parathyroid adenomata (1 Suspected clinically) (1 Detected microscopically)		2
			53	X	Thyroid removed for congestive cardiac failure		1		
III	Tumours		26						
	A Benign								
	Foetal adenomata	3							
	B Malignant								
	1 Primary	20							
	(a) Carcinomata	18							
	(b) Sarcoma	1							
	(c) Endothelioma	1							
	2 Secondary	3							
	(a) Carcinoma	1							
	(b) Sarcoma	2							
							102		

**TABLE III**  
**Sex and Age Incidence and Duration of Symptoms of Toxic Goitre**

Toxic Goitres	53	Males	16	Females	37
(1) Primary Toxic Goitres	37		10		27
(2) Secondary Toxic Goitres	16		6	„	10

T Y P E	Age in decades					Duration of symptoms in months									
	1	2	3	4	5	6	2	4	6	12	18	24	3	ys	
Primary	8	13	12	2	2	10	5	5	4	2	3	8			
	Duration of symptoms in years														
	3/4 1 2 3 4 5 10 & +														
Secondary	3	3	7	1	1	1	1	1	2	1	1	5	5		

**TABLE IV**  
**Evaluation of signs and symptoms of Toxic Goitres**

Type	Degree	Eyes Signs	Signs and symptoms C.V.S.	Obstruc- tion	Loss of weight	Alimen- tary system
Primary	+	12	9	16	11	4
	++	4	13	3		2
	+++			1		
Secondary	+	3	5	8	6	7
	++		3	2		
	+++		2			

Notes — Eye signs	Exophthalmos only	Exophthalmus with other eye signs	Marked Exo and eye signs
	+	++	+++
C.V.S.	Tachycardia only	Tachycardia and Palpitation	Thyro-cardiacs
	+	++	+++
C.N.S.	Tremors of Fingers	Fingers and tongue	Insanitary Hyper Excitability
	+	++	+++
Obstructive Phenomena	Swallowing	Swallowing and Breathing	Marked.
	+	++	+++
Loss of weight	Below 15 lbs	15 to 30 lbs	31 lbs and above
	+	++	+++
Alimentary system	Increased appetite	Diarrhoea	Both marked
	+	++	+++

TABLE V

The type, age and sex incidence, and duration of the Malignant Growths of Thyroid.  
No S/R confirmed by Section Reports 17

Serial No	TYPES	Total No	Age in decades						Sex		Duration of disease in years					Glands			
			1	2	3	4	5	6	M	F	1/4, 1/2	3/4	1	2	3		4	5	10&+
Primary																			
1	Papilliferous adeno Carcinoma	6			3	1	2		3	3	1	1	1		1	1	1	1	
2.	Carcinoma Thyroid	3			1		2		1	2	1				1			1	
3	Early Malignant Adenoma	3			1	1	1		3					1		1	1		
4	Endothelioma	1				1			1					1					
5	Sarcoma	1					1		1								1	1	
Secondary																			
1	Carcinoma	1				1			1								1		
2	Sarcoma	2			1	1			2		1			1					
1	Carcinoma Thyroid	6				2	3	1	3	3	2	1	1				2	3	
Total		23			6	7	9	1	11	12	4	3	2	2	3	1	2	5	5

TABLE VI

Pathological grouping of Malignant Tumours of the Thyroid.

<b>Group I Low or Potential Malignancy</b>	
(1)	Adenoma with blood vessel invasion
(2)	Papillary cyst adenoma with blood vessel invasion
(a)	Originating from Thyroid
(b)	Originating from Aberrant Thyroid
<b>Group II Moderate Malignancy</b>	
(1)	Papillary Adeno Carcinoma
(2)	Alveolar Adeno-Carcinoma
(3)	Hurthle cell Adeno-Carcinoma
<b>Group III High Malignancy</b>	
(1)	Small cell carcinoma (Carcinoma Simplex)
(2)	Giant cell Carcinoma
(3)	Epidermoid Carcinoma
(4)	Fibro Sarcoma
(5)	Lymphoma

## DISCUSSION

Dr E J Borges said I shall restrict myself in this discussion to a consideration of tumours of the thyroid I am very glad that Dr Munsif has drawn attention to a classification from the Lahey Clinic which he has placed here before us A classification to be satisfactory has not only to satisfy the pathologist but should also afford assistance to the harassed clinician in assessing the right treatment and prognosis of a particular case or group of cases In looking around for such a classification we found this one from the Lahey Clinic very useful and practical It is based, one might say, on two rather paradoxical features about the thyroid gland The thyroid gland is full of paradoxes We have all heard of the saying that the solid tumours of the thyroid often feel cystic and the cystic often solid The first of the paradoxes I am referring to is the fact that pathologists have found that the morphological characters of the cells in thyroid adenoma are unreliable by themselves for making a diagnosis of malignancy, so that it has often happened that a benign looking tumour has been shown later to have been malignant from the subsequent clinical history and vice versa Graham who has had a large experience of these tumours found, on reviewing a large series of adenomas and correlating their histology and subsequent clinical history, that the only criterion for



malignancy in an adenoma of the thyroid was the presence of blood vessel invasion by tumour cells whatever their morphology. This classification takes note of that. The second paradox I refer to is that whereas in other tumours there is a general rule that the more malignant are usually more radio-sensitive, in the tumours of the thyroid it appears to be just the opposite. The above-mentioned classification also takes note of that. By classifying his cases in this way the clinician is able to decide on the best treatment in each case and judge its prognosis.

#### CLASSIFICATION OF THYROID TUMOURS

##### BENIGN

- 1 Adenoma { Embryonal  
Foetal  
Colloid
- 2 Papillary cystadenoma

##### MALIGNANT

- Group I Low or potential malignancy—vary radio-sensitive
  - 1 Adenoma with blood vessel invasion
  - 2 Papillary cystadenoma with vessel invasion
- Group II Moderate malignancy—moderately radio sensitive
  - 1 Papillary adenocarcinoma—more radio sensitive than alveolar adenocarcinoma.
  - 2 Alveolar adenocarcinoma
  - 3 Hurthle cell adenocarcinoma
- Group III High malignancy—comparatively radio-resistant.
  - 1 Small cell carcinoma—least radio resistant of this group
  - 2 Giant cell carcinoma.
  - 3 Epidermoid carcinoma
  - 4 Fibrosarcoma
  - 5 Lymphoma (radiosensitive)

We have classified our cases according to this classification and I must say that it has been of great help to us as I shall hope to show.

#### CASES SEEN AT THE TATA MEMORIAL HOSPITAL IN 2½ YEARS

Benign tumours		
Colloid adenoma	18	All except 3 followed
Foetal adenoma	2	
Papillary cystadenoma	2	All well
Malignant tumours		
Group I	No cases seen	
Group II	12 cases	
Papillary adenocarcinoma	7 cases	
		10 cases

Of these only one was fully treated. Case No 1180 Mrs B aged 45, had a thyroid lump excised by a surgeon in Bombay in 1938. Kept well until 1940 recurrence then and came to us in 1941 and was found to have a nodule one inch in diam. Fixed to the trachea, and an enlarged and hard right lobe of the thyroid. Only nodule excised and found to be a papillary adenocarcinoma. As radiosensitive treated with X rays with remarkable success. Patient seen last month without evidence of disease for 3 years. This case illustrates how the histology indicated the treatment and prognosis.

##### Alveolar adenocarcinoma 5 cases

All advanced and all dead. As an example Case No 790 woman of 52 with a goitre of 5 years came with a history of haemoptysis of 15 days' duration. Hard swelling of the thyroid right lobe partly fixed to the trachea. Thyroidectomy done and tumour shaved off trachea. Pathology adenocarcinoma dead 3 months later.

##### Group III 1 case

Giant cell tumour. Case No 6321 Mrs D, aged 50. 6 months history of rapidly growing thyroid swelling with lymph gland metastases to one side. Thyroidectomy plus radical neck dissection on one side done at one sitting 3 months ago. Pathology as above. Decided against post-operative X ray as not radio-sensitive and also highly malignant with average life history of 9 months. Patient seen two months ago no recurrence then. Follow up awaited with interest.

Diagnosed as carcinoma on aspiration biopsy. 2 cases. One refused formal biopsy and has been treated outside with X rays. We are told he is well for the last 8 months.

##### Other malignant tumours

1 Spindle cell tumour, probably a variety of adenocarcinoma advanced and not treated.  
2 Hodgkin's disease of the thyroid. Very rare condition mentioned in literature. Case No 3902 Mr G J, age 37. 3 months suffocation and change of voice and dysphagia. Hard symmetrical swelling of thyroid typical of 'Woody Thyroiditis'. Isthmus excised to relieve respiratory distress. Histology of Hodgkin's disease. Patient died from haemorrhage from ulceration into oesophagus.

I shall say a few words about the diagnosis and treatment of thyroid tumours. First of all I must point out that aspiration biopsy is not of as much use as in other tumours for the simple reason already

mentioned that in the adenomas the morphology of the cells does not help. Of course, in the frank carcinomas it is possible to recognise malignancy but no classification is possible and therefore no indication for treatment is given. We do not advocate a formal biopsy in all cases for reasons that will be mentioned below.

*Treatment*—It will be generally agreed that a real adenoma (not the colloid adenoma of adenomatous goitre) should be speedily removed as it has so frequently been stressed that about 90 per cent of thyroid cancers arise in a previous adenoma. We also feel that all persistent thyroid swellings should be removed as we have seen quite a few goitres of several years' standing becoming malignant.

As for malignant thyroids we adopt the following attitude. If operable a radical thyroidectomy is done which includes a segment of the int. jugular vein and its thyroid radicals on the side of malignancy. If very adherent to the trachea the tumour is shaved off even if it is necessary to cut through tumour. On the histology found, the subsequent treatment and prognosis is founded.

If inoperable a formal biopsy is taken as the risk of breaking through the capsule does not matter in these advanced cases. If histology shows a radiosensitive tumour the appropriate course of radiation is given, after removal of as much of the thyroid as is possible to remove. If radioresistant palliative X-rays are tried without previous partial removal.

There is only one word more and that is about the adenoma that Dr Munsif mentioned which was adherent to the praetracheal muscles though histologically found to be benign. I should like to ask if the question of blood vessel invasion was considered in declaring the adenoma benign as in these treacherous adenomas things like local infiltration and adhesions are more important in assessing malignancy than the mere character of the cells."

Dr R. G. Dhayagude remarked that he agreed with Dr Borges that the thyroid pathology was full of paradoxes. He found it enigmatical in regard to the histological diagnosis of the tissues from gland. This difficulty was particularly felt in connection with the so-called toxic adenomas which histologically did not differ from adenomatous nodules in a goitre which was non-toxic. Even the histological diagnosis of the gland in Graves's disease was complicated by the administration of iodine which might produce so marked a regression in the hyperplastic picture as to resemble a simple goitre. The notes supplied with the specimen never made any mention whether iodine had been previously administered or not, nor did they give adequate information of the nature of the thyroid gland at operation or the operative procedure. Dr Munsif made a reference to sarcoma and endothelioma mentioned in pathologic material from the department. The diagnosis of sarcoma was based on a biopsy specimen as histologically it showed all characters of sarcoma. Recent work has shown that what formerly used to be called sarcomata are in fact carcinoma as judged when all the biological characters of the growth are taken into consideration. Since the whole gland was not

available for examination and further details were not supplied it has been allowed to remain in the category of sarcoma on histologic basis

The specimen of endothelioma was sent with a clinical diagnosis of goitre but no thyroid tissue was seen in it. The material showed unmistakable microscopic features of a vascular growth probably endothelioma infiltrating into striated muscle. It was grouped amongst the thyroid material but when all the evidence was put together it appeared to be that probably some wrong material was sent under this caption.

A word about the classification of tumours. It must be at once stated that the classification suggested from Lahey Clinic was useful for the clinicians in the present state of our knowledge. It did not however solve the difficulties of the microscopist. It is only a rearrangement of the material and from the thyroid material kept in the department it would be possible to regroup it in any suitable classification such as the one that suggested or any other that might be evolved hereafter as we come to know more about the natural history of the thyroid.

Dr R N Cooper said that he found rectal administration of paraldehyde to be a very suitable pre-operative sedative. He preferred to do all the thyroid operations with infiltration of 1 per cent novocain. Should the patient become restless during the operation he injected 5-10 cc of paraldehyde intramuscularly. For all subtotal thyroidectomies he routinely administered a blood-transfusion by the drip method during the course of the operation by dissecting out the ankle-vein. About 300-350 cc of matched blood were sufficient. Blood so administered constituted a very important safety factor in the operation. Multiple stage operations were recommended by so great an authority as Lahey of Boston. Lahey taught that the first impressions of a surgeon on seeing a case should carry great weight in the final decision for an operative procedure. If at the first consultation, the surgeon believes that a multiple stage operation is indicated, he should stick to that decision. The mortality rate at the Lahey Clinic was remarkably low and he attributed it to the large number of multiple stage operations done there. He discussed the other factors of safety such as the estimation of blood iodine, blood cholesterol and asked for a closer co-operation of the different departments to ensure better results. Injury to the recurrent laryngeal nerve was best avoided by exposing and identifying the nerve on every occasion.

Dr N D Patel said that the management of a case of exophthalmic goitre was always a difficult problem. The physician's chief anxiety was to decide when to call in surgical aid. One must not forget that with rest, diet, and psychotherapy many cases improved or remained stationary for years. The etiology of Graves's disease was obscure. One must remember the part played by the hypothalamus or emotions in the causation of goitre,—what some authors have described as a cerebral type of Graves's disease. Again, a warning was necessary with regard to the use of iodine. A possibility of iodogenic

# The Indian Physician

VOL III NO 10

OCTOBER 1944

WHOLE NO 34

## Original Contributions

### ON JOINT-CAPSULE-CHONDROMATOSIS \*

By

Dozent Dr GEORGE POLITZER

( With 4 X Ray figures )

(From the Princess Surendra Kumari Memorial Central X Ray Institute, Patiala )

In 1900 *P Reichel* described a case of chondromatosis of the capsule of the knee joint. The first important publication in English language was by *Henderson and Jones*. There are about 2-3 dozens of articles on this disease distributed over various journals and archives. Nevertheless a detailed description of the disease inspite of the publicity it has gained so far is essential for the following reasons

1 Many authors tried to devise a scale of cases showing the development of the disease. They used one or the other exceptional manifestation of the disease for this purpose obscuring in this way the fact that at least 19 out of 20 cases show completely identical and typical features

2 *Kienboeck* (1916) and others stipulated hypothetical etiological connections between chondromata and sarcomata of the joint capsule creating the impression that there are some difficulties in distinguishing these two diseases and that chondromatosis is liable to malignant degeneration. Thus a clear description of the diagnostic symptoms which permit us to differentiate between the joint capsule chondromatosis and other diseases of the joints is essential

3 It is necessary to explain the therapy of the chondromatosis in detail as the name of the disease is to some extent misleading on account of the morphological and histological findings in these cases

The disease is considered to be an extreme rarity, but this is hardly true because of the material that I used in Vienna for the post-graduate courses in the American Medical Association contained not less than 7 elbow joints, 3 knee joints and one shoulder joint affected by this disease. Ever since I am in India I found one case of the elbow joint and one of the knee joint. The latter—concerning

\* Condensed from a paper read at the Punjab States Health & Medical Conference Kapurthala on 9th August 1944

the brother of a famous Indian politician—is of special interest as he has been examined by many radiologists in India and England, none of whom diagnosing the case correctly

*Figure 1* shows a lateral view of the knee joint of this patient. The cavity of the knee joint is dilated. It contains a huge amount of small round bodies, whose outlines are marked by a thin calcified capsule but there are also calcified spots in the centre. They combine to bigger shadow units. In other cases (*Fig 2*) the number of the calcified bodies is by far smaller but their size is quite remarkable. The big bodies in *Fig 2* show the same kind of calcification as the small ones in *Fig 1*. While the bodies in *Fig 1* fill especially the joint cavity itself, the majority of the bodies in *Fig 2* lie in the suprapatellar



*Fig 1.*



*Fig 2*

lar bursa. *Fig 3* shows an elbow joint, in which again some calcified bodies are present, but they are not easily to be seen as the calcified capsule is very thin. In another case concerning the shoulder joint, whose picture I am not reproducing in this paper, the majority of the calcified bodies were localised in the sub-pectoral bursa. The bodies themselves were so heavily calcified through and through that their structure became quite homogeneous.

The clinical symptoms corresponding to these X-ray pictures are depending mostly on three factors

- 1 The joints affected by this disease are usually the knee and elbow joints, occasionally the shoulder joint. Chondromatosis of the hip joint as described in one case by *Schinz* and *Uehlinger* are extreme

rarities Due to the function of the joints concerned it is quite clear that changes in the elbow joint will trouble the patient by far less than affections of the knee joint, which may impede the gait already at an early stage of development

2 The examination of the resected capsule shows that even in cases, in which only a few calcified bodies are visible, there is hardly any spot of the capsule which can be considered as normal Some parts are thickened, some others carry half globe shaped tumours bulging into the joint cavity Other tumours are connected by a stalk with the surface of the synovial membrane and one or the other of the tumours may have lost the connection with its matrix entirely and floats as a free body in the joint cavity If free bodies are present, they may interpose themselves between the joint constituents and block suddenly the movements entirely

If the changes of the joint capsule are steadily progressing, ultimately the stage will be reached that is so well represented in *Fig 1* The joint cavity being completely filled with bodies of various sizes does not permit the movements of the joint any more for sheer lack of space This inability to move the joint combines with heavy pain caused by the interposition of these tumours between the facets of the joint constituents The question how far the joint capsule is involved and how much space is still left, should not be decided by consulting the X-Ray pictures alone Histological sections as made by several authors and by myself prove the very important fact that these joint capsule chondromata are not consisting of cartilage only They contain necrotic centres filled with deposits of lime salts, connective tissue, fat tissue, fibrous strands and blood vessels The visibility of these tumours in the X-ray picture depends on the lime deposits only and it can be stated that the calcified bodies visible in the X-ray picture are only a larger or smaller fraction of the real number present in the joint

In spite of the small variations described above, the X-Ray picture of the joint capsule chondromatosis is characterised by great uniformity and only one occasional divergence may be stressed, because it is of some clinical importance There are cases like *Fig 1* and *3* where the tumours lie in the joint cavity and others like *Fig 2* where they are mostly localised in bursae communicating with the joint Although in all these cases the synovial membrane is affected as a whole the changes are more advanced either in the main cavity or in the bursae The tumours in the bursae impede the movability of the joints less and cause thus often only minor troubles to the patient

Apart from these typical pictures one or the other case is mentioned in the literature in which only one chondroma is said to be present None of these cases—as far as I know—has been examined anatomically As the visibility of the chondromata depends on their incrustation with lime salts it cannot be excluded how many non-calcified chondromata were present simultaneously But apart from that, these cases are such rarities that they can be practically neglected

As far as the differential diagnosis is concerned the most essential question is, how far these chondromata can be distinguished from joint capsule sarcomata. It is quite evident that a sarcoma will not be visible as long as it does not either invade the bones, creating thus the defects typical for osteoclastic tumours or as long as it is not calcified in itself. Cases invisible to the radiologist are extremely rare. The diagnosis of the bone destruction by joint sarcomata is so easy that it does not need any detailed description. But something is to be said about the sarcomata of the fibrous capsule of the joints which can be diagnosed extremely early. *Fig 4* shows the X-Ray picture of an elbow joint\*. On the lateral surface of the fibrous capsule of the joint some calcified depositions are visible which form small spots and thin strands perpendicular to the surface of the joint. There is a well-marked localised tumour like swelling of the soft tissues of the lateral side of the elbow, in whose centre the above described calcifications lie. This type of joint capsule sarcoma is rare but so

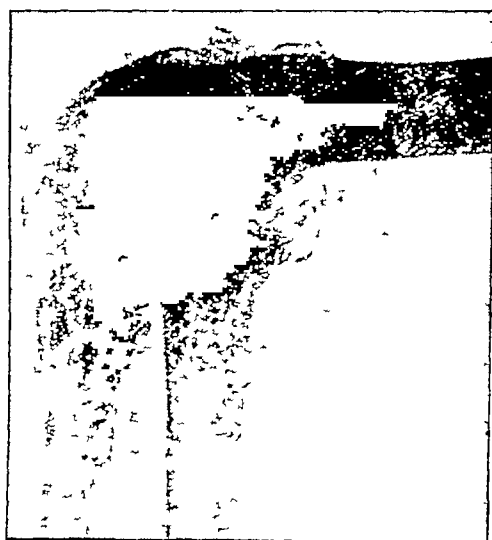


Fig 3

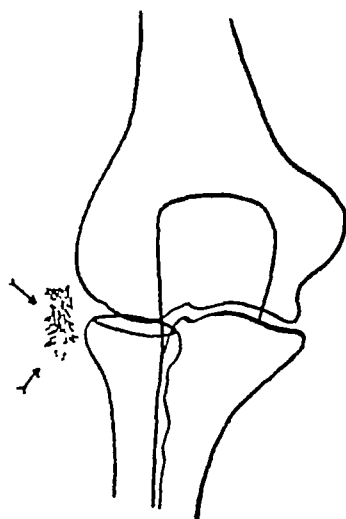


Fig 4

typical that no biopsy is necessary to confirm the diagnosis. In the case of *Fig 4*, I ordered the amputation of the arm without any preliminary biopsy. The histological examination of the preparation gained by the operation confirmed the diagnosis. The patient was alive several years after the amputation.

The joint capsule osteomata are rarer than the chondromatosis. In the majority of the cases they are singular and localised into the ligamentum patellae proprium or the fibrous capsule on its both sides. It looks in these cases as if one patella would be present above the other (*Kienboeck 1924*). Other localisations and multiplicity

\* The difference in density between the calcifications in the tumour and the bones is so great, that although the changes are well visible in the original film they are hardly recognizable in the copy. I therefore reproduce a diagram instead of a photograph.

(Kienboeck and Selka, Weiss) are rare. But even in these cases contrary to the conditions of the chondromatosis the capsule between the osteomata is normal. Therefore plastic operations are sometimes possible. The differential diagnosis against chondromata is easy as the former show typical bone structure while the latter are characterised by capsular and central lime incrustation of homogeneous structure.

Free bodies in the joint consisting of bone are found under various conditions. After fractures, osteochondritis dissecans or in severe cases of arthrosis deformans. In the first two conditions the bone structure of the free bodies and the defects in the facets whence the bone pieces have been broken out make the diagnosis very easy. Only the bodies in cases of arthrosis deformans must be discussed with a few words. Every case of chondromatosis leads earlier or later to arthrosis deformans due to the chronic irritation of the facets by chondromata. But in all these cases the chondromata predominate the picture, while the exostoses at the borders of the constituents are not attaining any size and extension comparable to them. On the other hand free bodies in cases of arthrosis deformans are found only in extremely severe cases so that here the massive exostoses are by far more impressive than the small pieces of bone which may have detached themselves. Other calcifications as the spontaneous lime incrustation of the menisci of the knee joint or the secondary calcification of parts of the menisci after trauma, the Stieda-shadow of the knee joint, the post-traumatical calcification as typical for the lower portion of the capsule of the shoulder joint also can hardly be mistaken for joint capsule chondromata or sarcomata.

As far as the therapy is concerned, it must be taken in mind that the joint capsule chondromatosis affects the capsule as a whole already in an early stage. In cases in which a free body blocks the movements of the joint and causes pain the removal of it is indicated. But it must be remembered that the same accident will occur shortly after the operation again. A radical operation means removal of the joint as a whole either by resection or by amputation and many cases especially those concerning the knee joint are gladly consenting to the operation fed up with the continuous troubles and preferring an artificial leg to a useless natural one. X-Ray therapy is without any value as proved by clinical experiences as well as by the common knowledge that connective tissue and cartilage are of a very low radiosensitivity. Electro-physical treatment gives only temporary relief. A contraption which sometimes is of some value consists of two padded leather bandages one round the thigh and one round the calf, both interconnected by two strong nickel- or chrome-plated steelbars on each side of the knee joint. A consolation for the patient, which shall not be omitted to be mentioned, is the fact that the disease remains usually restricted to one joint only and that it shows no tendency towards malignant degeneration.



## CONCLUSIONS

The joint capsule chondromatosis affects one joint only mostly the elbow or knee joint

Special stress is laid on the fact that in such a joint the whole capsule is involved although sometimes the majority of the tumours may remain undetected due to the lack of calcified elements in them

The differential diagnosis between joint capsule sarcomata and other joint diseases is described in detail

The therapeutic difficulties in these cases are explained and amputation or resection is recommended as the only successful treatment of advanced cases especially of the knee joint

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# Society Proceedings

The 40th meeting of the Seth G S Medical College Staff Society was held on Saturday the 19th August, 1944 in the Main Lecture Theatre of the College Dr N D Patel was in the chair Dr V N Patwardhan read a paper on

## BASAL METABOLISM OF INDIANS

In India the problem of basal metabolism has received a great deal of attention during the last fifteen years The Basal Metabolic Rates (henceforth mentioned as B.M.R.) of Indian men, women and children have been investigated by several workers in different parts of the country With the exception of a solitary investigator, the rest are all agreed upon the fact that the B.M.R. of Indians is lower than the values predictable by the Aub-Dubois, Harris-Benedict or Mayo Clinic standards for individuals of corresponding height, weight, age and sex The published Indian averages for B.M.R. of healthy adult males vary between 34.26 to 36.7 Cals per square metre per hour and for female adults between 31.2 to 32.05 Cals The differences between the average values are due to (1) the use of different types of apparatus, (2) the different personnel engaged and (3) the use of (a) only the first reading, (b) the average of a number of readings or (c) only the minimum reading for the calculation of series of averages The published figures for children show greater differences between the values published from the two laboratories (Roy and Wilson, *Indian Jour Med Res Niyogi et al Ibid*) which cannot be accounted for by any or all of the considerations mentioned above

The Bombay data, being of greater interest for clinical purposes locally have been treated statistically and the figures I and II give the means and the frequency distribution of the observations of (1) Sokhey and Malandkar (*Ind Jour Med Res* 27, p 501, 1939) and (2) Niyogi and Patwardhan with their associates Drs Powar, Mordecai and Sirsat (*Ind Jour Med Res* 27, p 99, 1939, *Ibid*, 28 p 345, 1940). A few unpublished observations on males and females from this institution have also been included The total number of males included in the analysis is 90 (58 subjects of Sokhey and 32 of Niyogi *et al*—1st series) and of females 57 (all of Niyogi *et al*) The ages covered by these subjects are from 19 to 40 in the case of males and 18 to 30 in females In the figures will be found the mean values, the standard deviation and the coefficient of variation etc It will be clear that the distribution around the mean is fairly balanced on both sides of the mean Since the mean value has been arrived at by using a mixture of first satisfactory reading (Sokhey) and averages of first day's observations only (Niyogi) the figures are somewhat higher than the results published from this institution

The factors responsible for the low B.M.R. of Indians have been discussed by many Indian workers and put to experimental test by some of them The more important ones are (1) undernutrition, (2)

the presence of any physiological abnormality, (3) low protein metabolism, (4) low muscle tone in the tropics, (5) the tropical climate, and (6) race. No definite evidence has been brought forward to show that factors 1 to 4 have any responsibility in the matter. The tropical climate may have an effect of lowering the B.M.R. on an average by 5 per cent at best. Even this is not universally accepted. The difference, however, between the Indian values and the three accepted prediction standards is greater than 5 per cent. Most of the workers in India now agree that the racial factor may in part be responsible for the low B.M.R. of Indians.

## MALES

## FEMALES

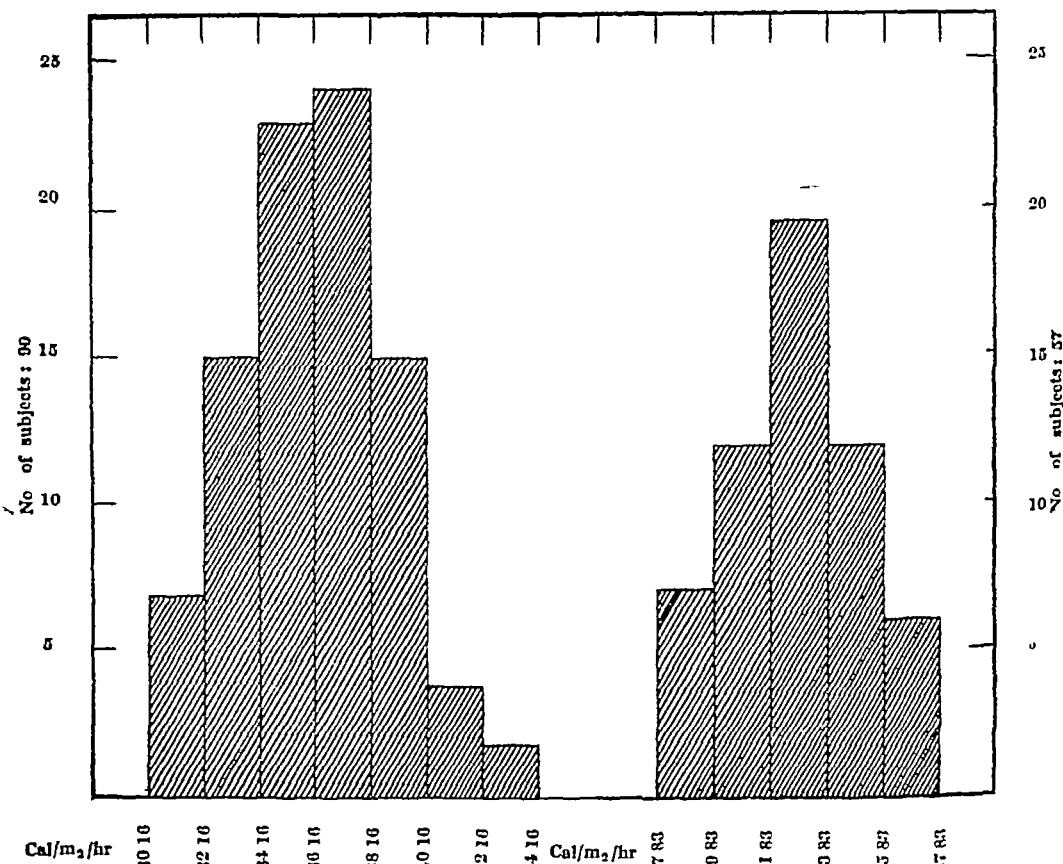


Fig. I—The B.M.R. of adult males in Bombay.  
Mean B.M.R. 36.16 Cal/m<sub>2</sub>/hr St. dev. 2.735 Coef  
ficient of variation 7.5 per cent.

Fig. II—The B.M.R. of adult females in Bombay.  
Mean B.M.R. 32.83 Cal/m<sub>2</sub>/hr St. dev. 2.45 Coef  
ficient of variation 7.46 per cent.

The survey of the published work shows very many gaps in the information. There is great scope for further work if filling up of these gaps were the only aim. Apart from that, however, a critical investigation on sound lines is needed to elucidate the role of the tropical climate, dietetic habits, occupation and race on the basal metabolic rate.

## DISCUSSION

Dr J G Parekh said, "I have been working on the problem of B.M.R. since 1937. We have studied a large number of normals and the patients coming from the Sir J J Group of Hospitals in the Physiology Department of the Grant Medical College. Our normal series comprised 79 subjects, 51 males and 28 females mostly from the medical students and members of the staff. The average caloric requirement per sq m per hour for males was 34.86 and females 31.6 a figure closely agreeing with that of Niyogi *et al* and being midway between those of Niyogi *et al* on the one hand and Sokhey *et al* on the other. We have taken the first reading as only one determination had been done in the majority of cases.

The pelidisi as per Von Pirquet Index in our series was 92.5 for males and 94 for females. The normal pelidisi is considered to be from 97 to 100. In view of the low pelidisi, it would be reasonable to say that our subjects were undernourished. The average weight of our subjects was 24 lbs less than English standards for the same age and height. Regarding the factors responsible for the B.M.R. of Indians race is not the only one but a number of other factors are also responsible. It has been mentioned by Dr Patwardhan that a hot climate causes reduction of B.M.R. by about 5 per cent. Besides this, under-nutrition, as shown by a lower pelidisi, the 'less tense way of life' and the lower protein consumption are all responsible for the lower B.M.R. of Indians. It is unfortunate that my figures have not been included in this study."

Prof R G Dhayagude wanted to know whether there were any differences in the apparatus used by Sokhey and Malandikar and Niyogi *et al*. He also wanted to know whether the different temperatures and humidity conditions at the time of B.M.R. determinations were responsible for difference in the average values reported by the abovementioned workers.

Dr N D Patel asked as to whether any investigations of B.M.R. on northern Indians and Europeans in India had been carried out.

Dr B N Purandare enquired if the effect of altitude on B.M.R. had been studied.

Dr M J Shah observed that seasonal variations of temperature and humidity in Bombay were not likely to affect the values of B.M.R.

Dr P Raghavan said that to date the clinicians had been calculating the caloric needs of their patients on the basis of 113 calories per lb body weight, as it has been shown that the B.M.R. of Indians is comparatively low, would it be necessary to take a low figure for meeting their caloric requirements?

Dr Patwardhan replied to the various questions asked during the course of discussion. In reply to Dr Parekh he said he was glad to note that Dr Parekh's results on B.M.R. of adult males and females agreed in general with those of other investigators in Bombay. The reason why Dr Parekh's figures were not included in the statistical analysis of the Bombay data was that Dr Parekh had not published them as the other two laboratories had done. He did not agree with the

contention of Dr Parekh that the figures of pelidisi indicated under-nutrition. Extensive investigations in China had shown that the pelidisi of the normal adult Chinese was nearer 90 than 100. Even in the case of Americans, Benedict observes that 94-95 is the figure more commonly found than 100. The published figures in India varied between 92 and 98 and they do not indicate undernutrition. It is true that a completely satisfactory test for the state of nutrition is still unavailable, but since the Pirquet's Index or pelidisi has been extensively used, the interpretation of its results obtained under comparable conditions may not lead one astray. In reply to the last question of Dr Parekh, it was said that the racial factor has not been held to be solely responsible for the low B.M.R. of Indians but as the most important one among many.

In reply to Prof Dhayagude it was pointed out that Sokhey and Malandkar used chain-compensated gasometer of Tissot type followed by analysis of the collected gases whereas Niyogi *et al* used a Benedict Roth type of apparatus in which only the oxygen consumption was estimated, the values for heat production being arrived at by assuming the R.Q. to be 0.82 and doing the necessary calculations. Between the temperature range at which the B.M.R. were determined no effect of the former on B.M.R. was expected.

In reply to Dr N. D. Patel, Dr Patwardhan said that with the exception of Banerji's work on convicts in Lucknow prison no other investigation on B.M.R. on North Indians has been reported. Regarding the observations on B.M.R. on Europeans in the tropics, it can be said that reports of many investigations are available but they are in the main inconclusive. Rajgopal at Coonoor compared the B.M.R. of Europeans and Indians, resident at the hill station, and he observed that the B.M.R. of Indians was lower than that of the Europeans.

Replying to Dr B. N. Purandare he said that the influence of altitude on B.M.R. had not been systematically studied.

The speaker agreed with Dr M. J. Shah that in Bombay no variation of B.M.R. with the season was observed. It may be due to the fact that the range of temperature change in Bombay throughout the year was very small.

In reply to Dr Raghavan it was pointed out that there was experimental evidence to show that even on weight basis the B.M.R. of Indians was low and that in their future calculations of dietary regime the clinicians would be justified in taking a lower figure than 11.3 Cals per lb of body weight as their basis. A figure for local use could be obtained by calculations based on the observations on healthy subjects investigated in Bombay.

Dr Patwardhan finally appealed to the clinicians to cease thinking in terms of Aub DuBois or Mayo Clinic standards and take as their base line the mean values reported in the Bombay series. As the majority of patients showing changes in B.M.R. due to disease and coming to the hospital for treatment belonged to the age groups which had been investigated in detail, such a comparison would be quite justifiable. It is hoped, however, that many lacunae pointed out this evening would be filled up in the near future.

# Critical Notes and Abstracts

## THE VALUE OF THE BLOOD SEDIMENTATION RATE IN RECOGNIZING DIARRHEAS DUE TO ORGANIC DISEASE

W C Alvarez, M.D., and J A. Barga, M.D., (Proc Staff Society of Mayo Clinic) A trying problem that not infrequently faces the consulting gastro-enterologist is to pick out quickly and surely from the many cases of functional diarrhea those few in which there is something organically wrong in the bowel, such as a regional stenosing enteritis, a beginning ulcerative colitis, a tuberculous or a cancerous lesion or a bacillary dysentery. During the last few years we have become more and more impressed by the fact that the blood sedimentation rate is of great help in this regard. If the figure is low, there is little chance that organic disease will be found, while if it is high, more than 40 or 50 mm in an hour (Westergren method), there almost certainly is something seriously wrong with the bowel. This observation has been made by others but it has not yet received the wide publication that it deserves and its importance and usefulness are not yet generally known.

On several occasions, when the appearance of the patient and the nature of the story led us to expect a nervous cause for a diarrhea, the finding of a high sedimentation rate immediately put us on our guard and caused us to insist that a careful roentgenologic study be made of the small bowel, a study that eventually revealed a previously missed lesion. On the other hand, we have had cases of diarrhea in which symptoms, such as fever, prostration and abdominal pain strongly suggested the presence of organic disease. Sometimes also the roentgenologic picture was suggestive of serious trouble but the findings of a low sedimentation rate warned us that we had better not explore the abdomen. In a few cases of this type in which, because of the seriousness of the illness or the insistence of the patient, exploration was made, nothing wrong was found.

Interestingly, the blood sedimentation rate is helpful also when it comes to estimating the extent or seriousness of colitis of the thrombo-vascular variety. In the patients in whom only the rectum and the sigmoid segment are involved, the rate may be within normal limits. The test appears to have value in determining the extent and severity of tissue destruction.

**SYPHILITIC ANGINA PECTORIS** Evans Jones and D E Bedford (British Heart J 5 2 107, April, 1943) analyse a series of 103 syphilitic patients with paroxysmal pain in the chest with special regard to the clinical characteristics of the pain and its pathogenesis.

Clinically the pain in syphilitic subjects is of two types (1) Angina of effort, and (2) Angina apart from effort. This latter is considered in detail under the following five headings:

(a) Nocturnal angina, (b) Spontaneous diurnal angina, (c) Angina

associated with paroxysmal dyspnoea (paradyspnoeic angina), (d) Syphilitic status anginosus, (e) Cardiac infarction syndrome

The age of onset of pain was evenly distributed over the fifth, sixth and seventh decades, its maximal incidence being actually between 40 and 50 years. There were 80 men and 23 women, giving a sex ratio 3.5 to 1. A history of syphilitic infection was obtained in 31 cases, the average period between infection and onset of pain was 24 years. A positive Wassermann reaction was recorded at some stage in 96 cases.

The main clinical findings were aortic incompetence in 67 cases, dilatation of the aorta in 59, cardiac enlargement, often slight, in 83, and essential hypertension in 26. Abnormal cardiograms were recorded in 57 of 94 cases examined.

76 patients were subject to angina of effort and 64 had pain apart from effort. Nocturnal attacks were common and were usually independent of paroxysmal dyspnoea. They tended to be prolonged but were relieved by nitrites. Paradyspnoeic anginal attacks occurred in 13, a syphilitic status anginosus in 9, and symptoms of coronary thrombosis, not attributed to syphilis, in 10 cases.

Post-mortem findings in 12 cases are given and other pathological data are considered. The essential lesions of syphilitic angina are aortitis and aortic incompetence, usually combined with stenosis or occlusion of the coronary ostia. Atheromatus and thrombotic coronary occlusion may be coincident with syphilitic aortitis. Pathological evidence that uncomplicated aortitis causes anginal pain is lacking.

The thesis of an atypical or pseudo-anginal syndrome due to aortitis is examined and rejected. Paroxysmal pain in syphilitic cases conforms to recognized clinical varieties of angina pectoris such as are encountered in non-syphilitic coronary and aortic disease. Aortic incompetence and obstruction of the coronary ostia, which affect the blood-supply to the whole heart, and cause widespread rather than focal cardiac ischaemia, predispose to spontaneous and prolonged pain. The horizontal posture appears to be an important exciting cause of these nocturnal attacks. In paradyspnoeic pain the effect of posture may be largely mechanical, but in other cases a reflex nervous mechanism may be operative. Consideration of certain cases also suggests that a relationship may exist between pressure pain from a dilated aorta and recumbency.

As to clinical course, prognosis and treatment of 103 cases, 37 have died, 21 are untraced, 45 were alive when the authors began to analyse these records before the war, and a few of them have been seen since. The average duration of life from the onset of anginal pain in the 37 dead was 24 years, 7 survived for more than 5 years, and one for 11 years. In the remaining 66 cases, 45 of which are alive and 21 untraced, the average duration of life from the onset of pain to the time they were last seen was 39 years. 27 of them have so far survived for more than 5 years and 5 for more than 10 years.

Though the expectation of life is appreciably less than in non-syphilitic angina, the outlook proved less gloomy, than has been

usually suggested American statistics (Levy, 1936) gives an average survival from the onset of symptoms in syphilitic aortitis of about 2 years or less, and German statistics are similar (Stadler, 1932)

With regard to the mode of death, 18 patients died in some form of anginal attack 7 of them had a terminal status anginosus and 5 were reported as having "symptoms of coronary thrombosis", 9 died in congestive failure, 6 died suddenly and in the remaining 4, no details were available

The effect of anti-syphilitic treatment was difficult to assess, but in general it did not remove the liability to anginal pain If due allowance was made for the effect of rest and other routine measures, it was difficult to be sure that specific treatment appreciably influenced the anginal symptoms In a few cases there was great improvement or even complete remission of symptoms for a time, and in a few others there was obvious aggravation of symptoms On the assumption that it checks the progress of syphilitic inflammation in the aorta and thus prolongs life, we believe that anti-syphilitic treatment should always be given a trial, but aggravation of symptoms indicates its immediate cessation Repetitive anginal attacks at rest or combined with paroxysmal dyspnoea are absolute contra-indications to anti-syphilitic treatment The ordinary measures applicable to angina pectoris, such as rest in bed, sedatives, and nitrites, should not be neglected

**CHRONIC FLEXNER DYSENTERY TREATED WITH SUCCINYL-SULFATHIAZOLE** Caldwell and Hardwick report (Lancet, 2 p 544, (Oct 30) 1943) the history of a woman aged 36 who had chronic schizophrenia She had had diarrhea and stools positive for Flexner dysentery intermittently for nearly eighteen months before succinyl-sulfathiazole therapy was instituted Sufaguanidine had been tried on four separate occasions without success Yet after a single course of succinylsulfathiazole her symptoms cleared and the stools became negative for the dysentery bacillus

**SULFAGUANIDINE IN SHIGA DYSENTERY** Guard describes (Medical Journal of Australia, 2 p 188, (Sept 4) 1943) the results of treatment in 25 cases of bacillary dysentery due to *Bacterium shigae* in New Guinea Although many patients with dysentery were admitted to the hospital during the campaign, shiga infections were not observed until the closing stages Since this type of dysentery is common in Japan, it is possible that the enemy was the source of infection The shiga dysentery encountered was on the average more severe than infections caused by *Bacterium flexneri* or the Boyd variety It is not, however, safe to predict the type of infecting organism from the symptoms In the treatment an initial dose of 2 or 4 drachms (75 or 15 cc) of sodium sulfate solution was given This was followed in two hours by 7 Gm (14 tablets) of sulfaguandine, then 35 Gm (7 tablets) was given every four hours Five doses were given each day until the number of stools in twenty-four hours was five or less, when the dose was reduced to 35 Gm three times a day until the number of stools was normal for two or three



days In severe cases with much dehydration and exhaustion the initial dose of saline solution was dispensed with and 7 Gm of sulfaguandine was given immediately, this dose was followed by 3.5 Gm given every four hours One-fourth of a grain of morphine and 1 one-hundredth of a grain of atropine were given in all cases associated with abdominal pain Fluids were given in the form of water, cordials, fruit drinks and barley water (from 4 to 6 pints a day) The patients were not starved The average period during which sulfaguandine was administered was 13.5 days Specific shiga antitoxic serum was not used, nor was it required No toxic effects were noticed which could be attributed to sulfaguandine, in spite of the large doses employed

**SULFONAMIDES IN DAMAGE OF LIVER** Peterson and his associates studied (*Archives of Internal Medicine*, 72 p 594 Nov 1943), the effects of the administration of sulfonamide compounds on the clinical course and hepatic function of 37 patients with various disorders of the liver All patients studied were admitted to Boston City Hospital Only those are considered in whom there was clinical and laboratory evidence of damage to the liver and in whom tests of hepatic function were made before and after a course of some sulfonamide compound Thirteen of the patients had acute hepatitis In all except 1 of these patients, who had a catarrhal jaundice, the damage to the liver was secondary to an acute pyogenic infection The remaining patients had chronic disease of the liver and included 14 with portal cirrhosis, 5 with biliary cirrhosis, 4 with damage to the liver resulting from chronic congestive cardiac failure and 1 with diffuse carcinomatosis To most of the patients the sulfonamide compound was given in the usual therapeutic doses and for a definite pyogenic infection To a few, however, the drug was given because of a suspected infection, the presence of which was not substantiated Sulfathiazole and sulfadiazine were each used alone for 14 patients, both were given in succession or on separate occasions to 7, and 2 received sulfapyridine The authors found that in the patients with acute hepatitis associated with bacterial infections the sulfonamide therapy was almost invariably associated with improvement in hepatic function which paralleled the improvement in the underlying infection In the patients with chronic damage to the liver, hepatic dysfunction was not aggravated by administration of sulfathiazole or sulfadiazine There was some improvement noted as a result of such therapy in cases in which bacterial infection was adding to the hepatic injury Severe toxic effects of sulfonamide therapy, other than direct injury to the liver, were usually frequent in the patients with portal cirrhosis and were twice as common after sulfathiazole as after sulfadiazine The authors conclude that the presence of damage to the liver should not be considered a contraindication to therapy with sulfathiazole or sulfadiazine in patients with bacterial infections against which these drugs are effective Sulfadiazine is the drug of choice in such cases Caution should be exercised in the administration of sulfonamide

compounds to patients with severe portal (Laennec's) cirrhosis of the liver

**THERAPY OF OPTIC NEURITIS WITH NICOTINIC ACID** Barrenechea and his collaborators employed (*Ophthalmologia Ibero Americana*, No 1, 5 p 7, 1943) nicotinic acid in 5 cases of optic neuritis. The disease was retrobulbar in 4 cases. It was of alcoholic origin in 2 cases, due to focal infection in 2 cases and secondary to mumps in 1 case. The drug was administered by mouth in doses of 50 mg each six times a day up to a daily total dose of 300 mg for ten consecutive days. In the course of the first twenty-four or forty-eight hours central vision and visual field improved, the central scotomas disappeared and the subjective symptoms stopped. The author believes that optic neuritis whether retrobulbar or not is due to local avitaminosis which results from the increased use of the vitamins, especially nicotinic acid, by the body owing either to local or general infection or to increased destruction of vitamins by bacterial toxins. Because of the fact that the good results of nicotinic acid therapy are not permanent as long as focal infection remains, it is advisable to carry on the proper examinations of the patient in the course of nicotinic acid therapy in order to control properly the infection after administration of nicotinic acid.

**THIOUREA IN TREATMENT OF THYROTOXICOSIS** Himsworth confirms Astwood's claims (*Lancet*, 2 p 465, (Oct 16) 1943), for the initial effects of thiourea in cases of thyrotoxicosis. Six cases have been treated. The author gives a detailed description of 1 severe case. The results in the other, milder cases were similar but less dramatic. In 1 case thyroidectomy was done because the goiter was compressing the trachea. In this case thiourea alone was given and proved a satisfactory preoperative preparation. The tissue removed at operation was hyperplastic and practically free from colloid. Two disadvantages have been found, and these have proved trivial. Thiourea has a nauseating taste, and at the beginning of therapy considerable nausea or even vomiting may occur. The second disadvantage is the peculiar sweet smell which it imparts to the breath. Discussing the mode of action of thiourea, the author says that the evidence at present available indicates that thiourea acts by interfering with the synthesis of the thyroid hormone.

**DIODOTYROSINE PREPARATIONS FOR HYPERTHYROIDISM** Pieber and Seyfried report (*Wiener klinische Wochenschrift*, 55 (p 46) (Jan 16) 1942), their experiences with intramuscular and intravenous injections of diiodotyrosine preparations in 20 cases of hyperthyroidism. Mild cases, particularly in the young, reacted exceedingly well. Peroral diiodotyrosine therapy has been tried with satisfactory results. One should not miss the optimum time at which to perform the operation in the more severe cases of hyperthyroidism. Conservative treatment with diiodotyrosine preparations gives satisfactory results, so that surgical intervention may be omitted in a considerable portion of the cases. Diiodotyrosine therapy is an excellent preparatory treatment to surgical intervention. It has the advantage over Plum-

mer's iodine therapy in that it may be stopped at any point. No untoward reactions will occur if the surgical intervention is postponed for some reason. Satisfactory results may be expected from the injections of diiodotyrosine in cases in which the Plummer treatment was ineffective or in which symptoms were caused by the delay of surgical intervention. Good subjective results were obtained in climacteric hyperthyroidism and in cases associated with severe hypertension and generalized arteriosclerosis. Twenty to 100 mg of the substance injected daily for from two to four weeks will produce no subjective reactions.

**LOCALIZED NEURITIS OF THE SHOULDER GIRDLE** According to Spillane, (*Lancet*, 2 p 532, (Oct 30) 1943), cases with unusual neuritic features have come to be recognized in the armed forces which were not observed before the war in such numbers. The author himself has seen 20 such cases, and he has studied the records of others. A fairly clear clinical picture emerged of what might be called localized neuritis of the shoulder girdle. In 42 of these 46 cases the onset of the illness was characterized by sharp pain about shoulder. The painful sites were usually along the upper border of the trapezius, over the spinati and the belly of the deltoid. Pain was sometimes felt along the inner border of the scapula, in the axilla or up the side of the neck. Many patients said it was severe and burning, and nearly all of them needed analgesics. The pain was commonly worse at night and disturbed or prevented sleep. It was aggravated by lying on the affected side and persisted acutely for from three to fourteen days, thereafter it rapidly subsided, but in a few cases a chronic ache was complained of for six or seven weeks. The pressure of braces or the weight of a gun or pack aggravated the discomfort. Pain was more severe in those muscles which subsequently showed atrophy. The muscles affected were the serratus magnus, spinati, deltoid, trapezius, sternomastoid and rhomboids. Effective movements of the shoulder girdle were greatly hampered. The wasted deltoid with paralysis of abduction, the hollowed supraspinous and infraspinous fossae of the scapula and the winging of the scapula, alone or in various combinations, produced a striking deformity of the shoulder girdle. The usual forms of treatment for neuritis did not seem to alter the course of the illness. If these patients are seen for the first time some months after the acute phase, the malady might be mistaken for poliomyelitis. The author differentiates the condition from poliomyelitis and also from acute brachial radiculitis or neuritis. He considers the possible role of injection neuritis and of repeated minor traumas. The preponderance of rightsided cases and the selective nature of the muscle wasting suggests that "injection neuritis" is not an important factor. It is quite possible that the long thoracic and suprascapular nerves could be injured by carrying a weight (pack and rifle) across the shoulder. Many of these patients, however, were employed in sedentary posts and 26 of them developed the illness while convalescing in hospital.

# A SCHEME FOR PERIODIC HEALTH EXAMINATION

*Mark all abnormalities in circles or in red*

DATE	NAME									
ADDRESS	AGE	M	F	S	M	W	D	RACE	RELIGION	NATIONALITY
	EDUCATION			OCCUPATION			Previous Present			

FAMILY HISTORY	age	health,	cause of death							
Pat	G F		Father				Brothers			
	G M									
Mat	G F		Mother				Sisters			
	G M						Children			

HEREDITARY DISEASES (including in uncles aunts, cousins)										
Nervous and Mental disorders						Epilepsy				
Cardiovascular						Blood				
Renal						Diabetes				
Allergy						Gout				
Gastrointestinal						Skin				
Neoplastic						Ears				
Endocrine						Eyes				

PAST HISTORY										
Diseases of childhood or infectious diseases										
Measles		Pertussis		Scarlet fever		Mumps		Diphtheria		Tonsillitis
Rheumatic fever		Chorea		Chicken pox		Small pox				
Encephalitis		Cerebrospinal fever		Pollomyelitis		Enteritis		Enteric fevers		
Dysentery		Jaundice		Malaria		Kalaazar		Ankylostomiasis Worms		
Inoculations		Vaccinia		TAB		Cholera		Plague		Rabies
Accidents and operations										Diphth
Hospital entries										Colds
Dyspepsia		Pepticulcer		Appendix						Pertussis
Nervous breakdown		H B P		Migraine		Neuralgias		Conv		Renal dis
Heart dis				Lungs		TB		Gono		Ducre
Sprue		Anemia		Furunculosis		Sinus		Ear discharge		LV Fistula

PERSONAL HISTORY	Preschool	School	Sex	Religion	Society
Home conditions	Congenital,	Depressing,	Alone in family		
Marital history	Financial status				
Working conditions	Interest in work	Hours of work	Sunlight	Noise	
Crowding	Dust	Dangerous chemicals	Sitting or standing	Fatigue	
Exercise	Recreations			Hobbies	
Mental State,					
Worries	Moods	Depression/Elation	Shock proof	Overprotected in childhood	
Attitude towards illness		Ability to make & hold friends			

APPETITE	Flatulence	gastric intestinal	Dental condition and treatment		
FOOD	Meats, Fish	Eggs, Dairy produce,	Grains	Pulses	Sweets
	Green veg, Salads, Fats, Fruits fresh, dry				
	Water	Tea	Coffee	Condiments	
FOOD ALLERGY			Tobacco	Drugs	Alcohol
BOWELS	Daily movement	with or without drugs	Kind of drug		
	Nature of stool				
URINE	F Day	Night	Pain	Nature of urine	
SLEEP	Hours	Feel rested	Morning fatigue	Dreams	
CATAMENIA	Regular	Interval	Days	Excessive/scanty flow	
	Dysparunia	Metrorrh	Menopause		
Pregnancies	Abortions	or misc	Stillbirths		Accidents

Foreign Travels	Service examinations
Insurance exam	Last Periodic exam

**REVIEW OF SYSTEMS****FEVER****PAIN****BREATHLESSNESS****LOSS OF WEIGHT****GEN WEAKNESS****FATIGUE**

Indigestion, Nausea, Vomiting, Anorexia, Fullness after food, Pyrosis, Dysphagia,  
Constipation, Diarrhoea, Tenesmus. Hiccough, Thirst Burning tongue or sore  
mouth. Jaundice

Cough Sputum, Haemoptysis, Suffocation, Hoarseness of voice.

Precordial pain Short of breath, Orthopnoea, Oedema, Palpitations

Nervousness, dizziness, headache, insomnia, convulsive or paralytic seizures, fainting  
or loss of consciousness, ataxia, loss of sensation, paraesthesia, numbness of  
fingers, cramps, twitchings

Memory changes, mental confusion, depression, excitement, compulsive ideas

Eyes Vision, night-blindness Ears noises, vertigo, deafness

**PRESENT COMPLAINTS** Mode of onset, duration and progress,**PRESENT STATE**

GENERAL	Posture	Height	Weight	W/H index	Ideal Wt
	Physique and constitution		Temp	Pulse	Resp
	Skin	Colour	Eruptions	Texture	Hair
<b>HEAD AND NECK</b>					
	<b>SKULL AND SCALP</b>				
	<b>EYES</b>				
	<b>EARS</b>				<b>MASTOIDS</b>
	<b>NOSE</b>				
	<b>FACE</b>				
	<b>MOUTH</b>	<b>LIPS</b>	<b>TEETH</b>	<b>GUMS</b>	<b>TONGUE</b>
		<b>INSIDE OF CHEEKS</b>		<b>TONSILS</b>	<b>PALATE</b>
<b>NECK</b>		<b>THYROID</b>		<b>Lymph nodes</b>	<b>Cervical</b>
					<b>Axillary</b>
					<b>Inguinal</b>

**THE CHEST****THORAX****BREASTS****LUNGS****HEART**

Exercise tolerance

Failure

Size of the Heart-Position of A B

Valves Heart Sounds and murmurs

Rate and Rhythm

Infection

Vessels B P

Aetiology

ABDOMEN  
LIVER

SPLEEN

PERINEUM  
RECTUM  
VAGINA

CERVIX

UTERUS

GENITOURINARY SYST

ADNEXA

P/V outlet

UPPER EXTREMITIES

Clubbing

LOWER EXTREMITIES  
JOINTS AND MUSCULATURE  
SPINE

ENDOCRINE STATUS  
METABOLIC DISORDERS  
DEFICIENCY STATES

# NERVOUS SYSTEM

Mental and Emotional state  
Speech

Aphasia

Apraxia

Posture

Right

Left

## SPECIAL SENSES

Vision  
Hearing  
Smell & Taste

## CRANIAL NERVES

## MOTOR SYSTEM

Contractures, Atrophy  
Invol movements  
Tone  
Vol power & movements  
Co-ordination, Ataxy  
Gait

## REFLEXES

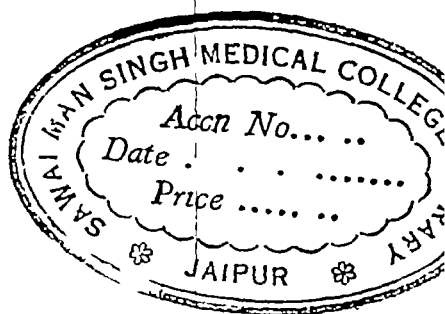
Deep B T S, H A  
Clonus  
Superficial Abd, Crem  
Planter

## SENSATION

Touch, Pain, Temp, Poslt, Vibr  
Stereognosis

## SPHINCTERS

## TROPHIC CHANGES



**MENTAL EXAMINATION**

Appearance, Attitude, Behaviour,

PERCEPTION Illusions Hallucinations

Disorientations

INTELLIGENCE Mental age Genius

Delusions Hypochondriasis

EMOTION Depression Elation

Phobias

VOLITION Inertia Psycho motor activity Compulsions

INSIGHT

**PERSONALITY TYPE**

Organic-Disease, Hypophrenic Isolation Schizoid, Cycloid

Psycho-Neurotic Antisocial

**LABORATORY INVESTIGATIONS**

URINE Date

STOOLS Date

BLOOD COUNT Date RBC Hb Gm% Hb% CI WBC P E B L M Parasites

SED RATE: Date

CULTURE Date

CHEMISTRY Date

SERUM:

WR

KAHN

WIDAL

BLOOD GROUP

COAGUL TIME

BLEEDING

FRAGILITY

PLATELETS

SPUTUM: Date

GASTRIC ANALYSIS: Date

X-RAYS: Date

E C G: Date

SPECIAL EXAMINATIONS: Date

C S F

B M R

FUNCTIONAL EFFICIENCY TESTS

**DIAGNOSIS**

Clinical

Acute

Chronic

Progressive

Morbid anatomical

Quiescent

Physiological (Functional Efficiency)

Psychological Personality Type

Aetiological

**DISCUSSION AND REMARKS****PROGRESS NOTES****TREATMENT**

Date

# The Indian Physician

VOL III NO 11

NOVEMBER 1944

WHOLE NO 35

## Original Contributions

### EVOLUTION OF A COMMON SEX SYMBOL

AS REVEALED IN A DREAM

*By*

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While analysing dreams it is not unusual to come across objects that stand as Sex Symbols, but it is not so frequently that one could trace the actual development of such symbols. That point is well brought out in the following dream.

A middle aged married man dreamt that while dressing he found that his genital organ was in an elongated and inflated condition and was almost touching the ground. Then immediately it separated from its base and like a reptile it began to creep rapidly on the floor in a snaky fashion and was about to fall out of the window of the first floor when he caught hold of it and putting it in its proper place he attempted rapidly to put on his trousers. But while he was doing so, it dropped down again and succeeded in swiftly creeping on the floor and then jumping out of the window into the garden. To his great dismay and fright he saw it joining other reptiles, like lizards and snakes, who were proceeding towards a small hut in the garden. He was terribly worried as he did not want to lose his organ. He dare not raise a cry for help because it was a delicate matter and he thought that other members of the household might accuse him of playing with his organ while he had not actually done so at that time. He hurriedly dressed himself and fumbled to get hold of a stick whereby he could stop and catch the precious organ which appeared like a reptile and was running away in a serpentine fashion. At this juncture he woke up.

#### POINTS OF INTEREST

1 Freud has often stressed the point of symbolism existing between the Penis and the Snake. The organ looked so snaky both in appearance and movements.

2 On analysing I found that this man was practising absolute continence both in thought and actions for past 3 weeks in order



that he may devote his attention heart and soul to the completion of a project in his hand

The detachment and the running away of the organ which he considered so precious a part of his body, are most probably an expression of his unconscious desire to renew his sex activities directly the project which he had undertaken was accomplished

3 So strong must have been his resolve for continence that the dream was not accompanied by any seminal discharge and erection

4 On waking up he thanked his stars that it was only a dream. During the dream he had felt that the task of recovering the run-away organ was almost an impossible one

5 In this dream one can trace up to a certain degree the evolution of the snake symbol. The patient sees his own organ elongating and running away like a snake and joining other similar reptiles. It is quite probable that later on the same patient would see snakes in his dreams which may be symbolically standing for his male organ, and not see the organ as such at all

# SIX CASES OF KALA-AZAR IN BOMBAY

## SODIUM ANTIMONY V GLUCONATE IN ITS TREATMENT

by

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BOMBAY

*History* Before the introduction in 1915 of potassium antimony tartrate in the treatment of Kala-azar, the disease was said to end fatally in 90 per cent of the cases. Since then the 90 per cent mortality has been converted into 90 per cent recovery. But the treatment was lengthy and the drug had many toxic effects. The next important advance was the introduction of pentavalent antimony aromatic compounds by Hans Schmidt (1916). Of these, para-amino-phenyl-stibinate (neostibosan) was the most successful and has been very widely used throughout the world. In 1922 Brahmachari introduced urea stlmanine, another preparation of para-amino-phenyl-stibnic acid, which he independently prepared in India. It is effective and is largely used here. Solustibosan (Bayer 561) a pentavalent antimony compound of the same class as neostibosan, but in a stable solution form, was introduced in 1937. On account of the war, this soon went out of the market along with other German preparations. In 1939, Yorke treated a case of Indian Kala-azar with stilbamidine. Since then it has been extensively tried in both Indian and Sudan Kala-azar. Sodium antimony V gluconate, the same compound as Bayer's solustibosan, is now manufactured by a British Pharmaceutical House, and is available in a 25 cc rubber-capped bottle, each cc containing 20 mg of antimony metal, for the treatment of Kala-azar. Here is an account of the treatment of six cases of the disease with this drug.

*The Patients* Kala-azar is a disease prevalent in the eastern half of India and not in this part of the country. Due, however, to a large influx of people into Bombay there were six cases of this disease admitted into the wards of the King Edward Memorial Hospital, Bombay, during the last 12 months. All of them were imported cases, three from the United Provinces, two from Bengal and one from Bihar. Of the affected persons two came to Bombay to seek medical help, three for employment and one a girl of 8 years came with her father who is now employed in Bombay.

*Diagnosis* The first two patients were in the hospital for some time before the disease was suspected. The suspicion arose from their having intermittent or continuous fever with enlargement of spleen and liver and from their having come from provinces where

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A paper read at the 41st meeting of G S Medical College Staff Society, Bombay, Sept 18, 1944, with Dr. A. Hameed in the chair.

Kala-azar is known to be endemic The following laboratory investigations were carried out —

(a) *Aldehyde Test* This test was strongly positive in four and very weakly positive in two In two other cases of splenomegaly admitted to the wards the same test was carried out It was repeatedly positive in a Pathan with enlargement of the spleen up to the umbilicus and pleurisy with effusion on the left side Leishman Donovan (L.D) bodies were not obtained either on smears or on culture even after two sternal and two splenic punctures Examination for serum protein showed a content of 4.49 per cent globulin and 2.2 per cent albumin In another man from the United Provinces, who had come to the hospital for fever of short duration and in whom the test was strongly positive, culture and smear from the sternal puncture fluid were negative In both of these cases, the aldehyde test was strongly positive, but the men were not suffering from Kala-azar The Pathan was treated unsuccessfully with sodium antimony V gluconate

(b) *Sternal Punctures* This was carried out in all cases The smear was positive in 4 cases and culture in all six Culture had to be done twice in two cases (Nos II & III) before L D bodies were grown Except in the single case mentioned above, treatment was started only after L D bodies had been found in smear or culture The disease was of moderate duration in 4 cases, of four weeks in one and of ten months in another In none of the cases had previous antimony treatment been given

*Treatment of the present series of cases* The treatment of the first case in this series was started cautiously with 2 c.c (One c.c containing 20 mg of antimony metal) on the first day and 4 c.c on the following days On the 4th day the dose was increased to 10 cc which was continued for 16 days with one day's interval, the total dosage given was 152 c.c in 19 days This dosage was tolerated without any general or local ill-effects and with apparent cure of the disease In the second case the dose was increased to 20 cc a day intravenously for 10 consecutive days making a total of 200 cc On the first day, 10 cc was given in the morning and 10 cc in the evening The patient tolerated the drug well and was apparently cured, hence it was decided to use 20 cc daily for 10 days in future In cases Nos III & IV, these being children under 60 lbs of weight, proportionately less was given, a total of 150 cc and 120 cc respectively In case No V, the total dosage was 200 cc in 10 days As the quantity to be injected was large the manufacturers, in order to reduce the bulk, prepared for experimental purposes, a more concentrated solution, 1 cc containing 50 mg of antimony metal, and this was used in case No VI, a boy of 15 years, 5 cc (in two doses of 2 cc in the morning and 3 cc in the evening) on the first day and 6 cc daily intramuscularly for 9 days making a total of 59 cc of sodium antimony V gluconate (containing 50 mg metal of antimony per cc)

*Ill-Effects* There were no ill-effects in any of them except

gingivitis in case No VI Case No I had bronchitic signs in the lungs (sulphapyridine given previously in the usual dosage had proved ineffective) which cleared up with the treatment In two other cases (Nos II & V) the albumin content of the urine practically disappeared with the treatment In these two cases, there was no other evidence of nephritis Cases Nos IV & VI had ascites with small quantity of fluid, which cleared up with antimony without the help of other treatment One case with splenomegaly and pleurisy with effusion, where the aldehyde test was repeatedly positive, but where both the sternal and splenic punctures were twice negative for the presence of L D bodies in smear or culture, was treated with 200 cc (20 cc x 10 days) with no increase in his lung condition or ill-effect on general health, thus showing that the drug has practically no toxic effects

**Progress** With treatment, the temperature in all but one of the cases settled down to normal between the 2nd and the 4th day The exception was case No I, where treatment was started with 2 cc, it came to normal on 7th day In all cases there were increase of body weight and reduction in size of spleen and liver at the end of treatment There were improvement in blood count (R. B C and Hb) and rise in total leucocyte count at the end of the treatment, except in case No V where the leucocyte count was normal

**Final Cure** There appears to be no immediate criterion of cure in this disease and time alone can indicate if an apparent cure is a complete cure In all these six cases the criteria for immediate cure were fulfilled (increase in weight, temperature dropping to normal, increase in white cell count, decrease in size of spleen and liver) Cultures of sternal puncture fluid were negative in all cases at the end of treatment, except in case No II, where it was positive after treatment, but negative six months later Cases Nos I and II have been followed up and have not relapsed more than six months after the completion of treatment Case No III died of T B meningitis four months after the completion of treatment, post-mortem yielded no evidence of Kala-azar Cases Nos IV & V have not relapsed five months and four months respectively after the completion of treatment Sufficient time has not elapsed to judge the final cure in case No VI. Data of the 6 cases of Kala-azar are given in the Table (p 322) A few notes of each are given below

Case No I was admitted with fever, marked anaemia and lung signs He was treated with quinine by injection, liver extract and blood transfusion for anaemia and sulphapyridine for bronchitis

Case No II was admitted for continuous fever, general debility and splenomegaly He had fever remittently but had been afebrile for some time It was during a febrile period that he was diagnosed He is still healthy nine months after the treatment, but his spleen is still palpable 2 fingers below the costal margin

Case No III had intermittent fever, splenomegaly and free fluid in the abdomen The fluid was less at the end of treatment, but it took three months to disappear completely During his stay in the hospital, he suffered from mumps and later from tuberculous meningitis Post mortem revealed normal liver, but the spleen (not palpable anti-mortem) was lightly enlarged. L. D bodies were not seen in smears from the liver or spleen The liver showed some patches of subacute necrosis

Case No IV had been suspected for typhoid before she was diagnosed.

Case No V has greatly improved with treatment and has put on 20 lbs of weight in 4 months

Case No. VI had ascites. He has increased 7 lbs in weight, but has still to be followed up

T A B L E

Case No. & Date	I Dec 1943	II Dec. 1943	III February 1944	IV March 1944	V April 1944	VI Aug 1944
Age, Sex, Province	25 Male United Province	40 Male Bengal	10 male United Province	8 Female Bihar	30 Male Bengal	14 Male United Province
Duration of illness	3 months	4 months	4 months	2½ months	1 month	10 months
Weight	On admission 106 lbs. On discharge Not taken	On admission 93 lbs. On discharge 95 lbs.	On admission 47 lbs. On discharge 54 lbs. (in 10 days) later	On admission 37 lbs. On discharge 42 lbs.	On admission 60 lbs. On discharge 92 lbs.	On admission 42 lbs. On discharge 40 lbs.
Nature of temperature	Intermittent 7th day 1 finger Just palpable	Remittent 3 fingers + + + + + 7 fingers	Intermittent 3 fingers + + + + + 6 fingers	Continuous & intermittent 1½ fingers 4 fingers	Intermittent 2 fingers + + + + + 7 fingers	Intermittent 3½ fingers 6 fingers
Liver	2 fingers	Strongly + ve	Strongly + ve	faintly + ve	faintly + ve	++
Spleen	3 fingers	Weakly + ve	Weakly + ve	faintly + ve	faintly + ve	++
Blood : Aldehyde Test	Strongly + ve	Strongly + ve	Strongly + ve	faintly + ve	faintly + ve	++
RBC	1 08 mill.	Not done	2 70 mill	3 20 mill	1 88 mill	3 00 mill
WBC	1000	5100	3100	4000	8,200	2,400
Diff Count. P	40%	60%	47%	66%	32%	50%
Count. L	67%	Not done	70%	70%	32%	34%
E	24%	33%	47%	36%	0%	0%
LM	3%	1%	3%	4%	1%	2%
Diagnostic Punctures	1) smear + ve 2) culture + ve	Not done	Not done	Not done	Not done	Not done
Sternal P 1 Smear	1) smear + ve	Not done	Not done	Not done	Not done	Not done
2 Culture	2) culture + ve	Not done	Not done	Not done	Not done	Not done
Urine	Alb. + + + +	Alb. + + + +	Alb. nil	normal	normal	normal
Treatment	Started with 3 cc. 153 cc. in 10 days. I V route 10 cc. maximum (3 Gm)	30 cc. per day i v 200 cc in 13 days given in 10 injections.	15 cc per day i v for 10 days total 160 cc. (3 Gm)	12 cc per day i v for 10 days 120 cc total. (2 ½ Gm.)	20 cc. per day i m for 10 days—200 cc total (4 Gm)	5 cc. 1st day 6 cc. (50 mgm antimony per cc.) daily 1m for 9 days 50 cc total (3 Gm)
Toxic effects	nil	nil	nil	nil	nil	Gingivitis
Cure	nil	yes	cure	yes	yes	yes
Apparent	Healthy 8 months later	Healthy 8 months later	Healthy 8 months later	Healthy 8 months later	Healthy 5 months later	To be followed up
Final	Healthy 8 months later	Healthy 8 months later	Healthy 8 months later	Healthy 8 months later	Healthy 5 months later	To be followed up

## DISCUSSION

*Pharmacology of Sodium Antimony V Gluconate* It is a clear colourless stable solution and is available in sterile bottles containing 20 mg of antimony (metal) per cc as against 21 mg of antimony in one cc of 5 per cent solution of neostibosan. It can be given intramuscularly or subcutaneously. Weese (1937) reported that the drug is more rapidly excreted in experimental animals than neostibosan. In dogs 80 per cent of the drug is excreted in the first 24 hours as against 50 per cent neostibosan and therefore the effect is not likely to be cumulative. Goodwin & Page (1943) state that both in experimental animals (mice and rabbits) and in human beings "the most rapidly excreted antimonial in the quinquevalent group is sodium antimony V gluconate—next in order come stibacetin, stibamine glucoside (neostam), urea stibamine and neostibosan, though there is little to choose between them—60 per cent to 80 per cent of the drug was excreted in the first six hours and 80 per cent to 90 per cent in twenty four hours". They also found that antimony disappears from peripheral blood within three hours of the injection of sodium antimony V gluconate, and that larger doses of sodium antimony V gluconate were excreted at a higher initial rate than smaller ones especially after intravenous injection. By the end of 48 hours the excretion is complete. Weese (1938) suggests that larger doses flood the whole body and the 'overflow' is excreted very rapidly, the amount of overflow depending upon the amount injected. This suggests that the effectiveness of the sodium antimony V gluconate is not proportionately increased with higher dosage.

*Toxicology* Sodium antimony V gluconate is very similar to neostibosan, being less toxic than the latter weight for weight, of antimony, when given subcutaneously and distinctly less toxic when given intravenously, 18.5 cc (370 mg of Sb) per kgm is the lethal intravenous dose for a mouse against 6 cc of a 5 per cent solution of neostibosan (126 mg of Sb) (Napier 1937), that is to say the mouse will survive an intravenous dose of sodium antimony V gluconate representing three times the amount of antimony in the tolerated doses of neostibosan. That the toxicity of sodium antimony V gluconate is less may probably be due to its rapid excretion as shown above (Goodwin & Page 1943). Sodium antimony V gluconate has shown no toxic effects in human beings too. All the previous workers have noticed its innocuousness in the treatment of Kala-azar. In the present series of cases, the drug had no toxic effects—anaemia (Case No I) which had failed to respond to blood transfusion, was mitigated by treatment. Ascites (Cases Nos III & VI) and albumin in urine (Cases Nos I & VI) diminished rapidly under treatment. Conditions, such as severe anaemia, ascites and nephritis in advanced cases of Kala-azar, which used to be aggravated by antimony treatment can safely be treated with sodium antimony V gluconate. Hatt (1944) reports that 3 cases of advanced kala-azar with ascites cleared up with treatment with sodium antimony V gluconate, a mercurial diuretic being given as an adjuvant treatment. In one

of his cases of kala-azar with severe anaemia (Hb 15 per cent, RBC 0.98 million per cm.m) the drug not only had no adverse effect but a regenerative one, which he could never, in his large experience, have expected with other antimony preparations. Kikuth and Schmidt (1938) found that in experimental Leishmaniasis of the European hamster (*Cricetus cricetus*) the amount of metallic antimony necessary to bring about a cure with sodium antimony V gluconate was somewhat greater than with the case of neostibosan. They found the effective dose of sodium antimony V gluconate to be 65 cc (130 mg of Sb) as compared to 200 mg of neostibosan (containing 89 mg of Sb). The fact that large doses of antimony are required in the form of sodium antimony V gluconate compared with those in the form of neostibosan is probably due to its rapid excretion (Goodwin & Page loc cit). This seems to indicate that in terms of antimony content, larger doses of sodium antimony V gluconate are necessary to cure human cases of Kala-azar as compared with those of neostibosan. Struthers & Lin (1937) used a total of 59 cc to 85 cc of solustibosan daily or on alternative days and reported a cure rate of 22 out of 26 cases. Yates (1937) used 12 cc daily (using 20 cc maximum in some cases) for 5 days without any toxic symptoms. He claimed to have cured 78 out of 82 cases. Napier et al (1937) gave 10 injections intramuscularly on alternate days and in some cases daily, beginning with 2 cc and increasing up to 9 cc. He states that both the individual and total dosage had been arbitrarily chosen but admitted that largest individual dose given by him was only a small fraction of the largest dose relative, weight for weight, tolerated by animals. Ching et al (1942) cured 22 out of 24 cases with a total dosage of sodium antimony V gluconate of 60 cc to 162 cc. Napier and Sen Gupta (1943) reported 3 cases treated with sodium antimony V gluconate as not cured. This failure they ascribed to the drug not possessing anti-kala-azar activity comparable with neostibosan and urea stibamine. They, however, do not mention the dosage given.

So in the treatment of kala-azar with sodium antimony V gluconate, previous workers have used the drug in varying doses. Basing it on the usual dosage of other antimonials, they seem to have used it in quantities comparable, in terms of antimony metal, with those contained in neostibosan. The interval between the two injections has been similar. They seem to have completely ignored the rapidity of excretion of the drug as compared with other pentavalent antimonials in common use, with the result that the cure rate has varied greatly with different workers, some even going to the extent of stating that the drug is relatively ineffective as an anti-kala-azar remedy, but all of them agree on its innocuousness.

In view of the above reports, the treatment of the first case in this series started cautiously with 2 cc on the first day gradually increasing to a maximum of 10 cc a day. A total dosage of 152 cc was given without any ill-effects. For the second and subsequent cases, it was increased to 20 cc daily for 10 days. Children weighing less than 60 lbs were given proportionately less. These high doses

were administered with the idea of finding out the maximum quantity of the drug which could safely be tolerated. If this was ascertained the minimum effective dose could be found later. So far this is the largest dosage (given in 10 days) employed in India, though Burke and Chakarvarty (1944 June) have used a maximum of 150 cc of sodium antimony V gluconate (15 cc daily for 10 days) for an adult. Kikuth & Schmidt (1944 March) also advocated a daily dosage of 10-12 cc up to a total of 120 cc to 180 cc. They found that even a total maximum dosage of 240 cc could be given with safety. As the quantity to be injected with this higher dosages was large they tried out a more concentrated solution, with the result that two new preparations were established (1) an aqueous concentrated solution (1 cc containing 100 mg of antimony metal of sodium antimony V gluconate) which they claim was absorbed from the tissues without irritation, even though hypertonic and can be given intravenously and intramuscularly, and (2) a suspension of sodium antimony V gluconate powder (54 mg in one cc) in oil, which is very slowly absorbed from the oil depot so that body would be under the action of antimony for longer time. They further report that tests on kala-azar infected hamsters showed that eight injections of aqueous solution, involving the administration of 500 mg of sodium antimony V gluconate (not of antimony metal) per kgm of body weight, sufficed to bring about a cure, the same result was obtained by a single intramuscular injection of 6 cc (324 mg of Sb) of suspension per kgm of body weight. Roentgen ray examination showed that such an oil depot had been completely absorbed in 48 hours. The clinical trials carried out in China with oil suspension have shown cures with a smaller number of injections than with the aqueous solution. Ramos et al (1942) have used both concentrated solution and suspension in oil with success in 7 children suffering from Mediterranean kala-azar. Lozano (1943) has treated 5 cases of infantile kala-azar in Spain with concentrated solution (100 mg per cc) with marked success. There were no local or general reactions. In the light of this new evidence and the experiences in the treatment of the cases of the present series, it is suggested that the dosage of sodium antimony V gluconate for the treatment of Indian kala-azar should be between 3 gm to 4 gm of metallic antimony, i.e. 150 cc to 200 cc of 20 mg strength solution, or proportionately less of a more concentrated solution, given in 10 daily injections. In recent years, various non-antimonial remedies for kala-azar have been introduced. Starting in 1939, Warrington Yorke introduced 4,4-diamidino-stilbene in the treatment of kala-azar and by now more than 100 cases have been treated with the drug all over the world (Adams and Yorke (1939 & 1940), Kirk & Satl (1940 and 1940a), Napier & Sen (1940), Napier, Sen Gupta & Sen (1942)). Another diamidino compound (diamidino-di-phenoxy-pentane) has also been used (Napier & Sen Gupta 1943). From a careful examination of all these published reports, however, it is clear that although it is a remarkably effective anti-kala-azar remedy, even being effective in proved antimony resistant cases and in Sudan



kala-azar, which is less responsive to antimony than Indian or Chinese kala-azar, there is no doubt that the unpleasant and even alarming reactions experienced in the majority of cases make this drug unsuitable for general use, particularly for out-patient clinic work, where a large number of ambulatory cases have to be treated. Recently too, troublesome neuropathic sequelae have been reported (Napier and Sen Gupta 1942). On this subject, we find, in an editorial article (Indian Medical Gazette, 1943 April), the following conclusion —

“We must emphasise that the aromatic diamidines will not replace the pentavalent antimonials in the treatment of ordinary cases of Indian kala-azar, but that in diamidino-stilbene we have a remedy which holds out the best chances of cure in cases in which the antimonials have failed”

So for routine treatment pentavalent antimonials are preferred. Which should it be? Neostibosan has hitherto been the antimonial preferred by the majority of people. With the evidence presented above one would consider sodium antimony V gluconate to be the drug of choice because it has so many advantages over neostibosan and urea stibamine and it is suggested that it should be given extensive trials with increased dosage in endemic areas.

#### SUMMARY

- 1 Six cases of kala-azar admitted in the K. E. M. Hospital during the last 12 months (imported into Bombay) have been studied and treated with sodium antimony V gluconate, with immediate cure in all, complete cure in 5 and probable in one (in one treatment has just been completed).
- 2 The pharmacology of sodium antimony V gluconate, as regards its excretion and toxicology, has been reviewed. A scheme of higher dosage has been tried.
- 3 It should be given extensive trial in cases in endemic areas. It seems a suitable drug for mass treatment of kala-azar in India.
- 4 It is suggested that physicians should be on the look out for this condition in areas where kala-azar is not endemic, or is rare, and for that reason is unsuspected. A history of continuous or remittent fever, with enlarged spleen, in a person who is a native of Eastern India, or who has resided there, should be investigated with the possibility of kala-azar in mind.

I take this opportunity to thank all the Honorary Physicians of the K. E. M. Hospital for allowing me to treat and publish these cases. I appreciate very much the co-operation of the resident members of the staff. I am most grateful to Dr. B. M. Amin for carrying out the cultures of sputum puncture fluid. I thank Dr. V. N. Patwardhan for carrying out serum protein examination in one case. I thank Messrs. H. J. Foster & Co., Ltd. for the supply of Stilbatin (Glaxo Laboratories) generously given. My thanks are also due to the Dean, K. E. M. Hospital for permission to publish this paper.

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## DISCUSSION

Dr M J Shah remarked that the incidence of Kala azar in Assam was greater in non Hindus as the Hindus kept cows which attracted the sandflies. He asked whether comparative studies of various anti Kala azar drugs had been made in Bombay and whether a follow up of cases so treated had been carried out. He also asked for an explanation as to the work of Napier who had obtained good results in 1937 and poor ones in 1943

Dr P Naghavan said that he had observed an excessive appetite in his cases of Kala azar

Dr J K Mehta wanted to know whether a concentrated solution of sodium antimony gluconate was more effective in the treatment of Kala azar or whether it merely reduced the volume of fluid to be injected.

Dr A Hameed said that in the ordinary blood smears parasites might not be found, a better method being to make smears after centrifuging the blood with Locke's solution. He added that a splenic puncture was of a greater diagnostic value than the sternal smear. The former was to be resorted to if the sternal smears proved to be negative. A cultural examination of this material along with that of the blood was to be carried out as a routine. About the treatment he pointed out that in Sudan antimony compound were not found satisfactory whereas diaminodibenzene was found effective. This drug gave rise sometimes to toxic symptoms both of an immediate as well as of a delayed nature.

Dr J C Patel in reply to Dr M J Shah remarked that out of his cases 4 were Mohammedans and 2 were Hindus. He was not aware of their contact with cows. He also said that there was no possibility of a comparative study of various drugs being made in Bombay, where only a small series of imported cases were found. There were no reports in the literature of a follow up in the cases published. Napier in 1937 had definitely considered this drug as a distinct advance over Neostibosan. The poor results obtained by him in 1943 were probably due to insufficient dosage. In reply to the question of Dr J K Mehta the speaker said that in view of the rapid excretion of the drug large doses had to be administered for an effective cure large doses of 20 mgm. of antimony metal in 20 cc. were to be given preferably intramuscularly. To reduce the bulk a higher concentrated solution 50 mgm. of antimony metal was tried. The only advantage it had was of reducing the bulk, but it probably had the disadvantage of requiring a large amount of antimony in terms of metal than in the more diluted solutions.

## LABORATORY FINDINGS IN KALA AZAR

Dr B M Amin then presented the laboratory findings in 51 cases investigated for Kala-azar and dermal leishmaniasis during the course of the last eighteen months. He emphasised the importance of a definite diagnosis as a preliminary to the treatment of these diseases with specific drugs.

Twenty-five cases were investigated for Kala-azar, including one for post-Kala-azar dermal leishmaniasis. Of these, eight were diagnosed as Kala-azar by the demonstration of the parasites either in smears or in cultures, or both. The Formol-gel reaction was done in seven of these cases and was positive. In the case of post-Kala-azar dermal leishmaniasis the parasites were demonstrated only in the skin.

The results of the positive cases are tabulated below —

Case No	Formol gel reaction	Sternal marrow (Smear) (Culture)		Blood culture
1	Positive	Positive	Positive	Not done
2	"	Negative	"	"
3	"	"	"	"
4	"	Positive	"	Negative
5	"	Negative	"	Positive
6	"	Positive	"	"
7	Not done	Not done	"	Not done
8	Positive	Positive	Not done	Positive
9	Negative	Negative	Negative	Negative (Skin biopsy smear & culture positive)

The Formol-gel reaction was also found to be positive in four cases of chronic malaria and one of pleurisy

Out of the 26 cases investigated for Oriental sore, 18 were positive. In 16 of these, the diagnosis could be made from an examination of the smears. In two cases, the smears were negative and cultures positive. He pointed out that about half the number of cases contracted the infection in some town of Gujarat.

He then described the various laboratory methods used in the diagnosis of leishmaniasis and observed that in his experience the cultural methods were very reliable in the diagnosis of kala-azar.

(Continued from page 335)

tumour was removed. She came to this hospital on 28-6-44 with pain in the right shoulder and swelling. X-ray picture revealed metastasis in spine of right scapula. She was treated with X-radiation. The further course of the case is being watched. We were fortunate in getting the operated material since 1937 for histological study from the outside hospitals where the patient was previously operated. The histological appearance of the primary tumour showed an appearance of adenosarcoma. With subsequent recurrence the histology of the tumour presented more anaplastic characters and assumed the characters of a pure sarcoma with spindle-shaped cells. The metastatic tumour in the ovary showed structure of spindle cell sarcoma.

Dr Sirsat said that sarcoma of the breast can be divided into two main classes: (1) Adenosarcoma and (2) Pure sarcoma. The most common type is the adenocarcinoma in which the malignant transformation of connective tissue is accompanied by the presence of epithelial elements. In pure sarcoma no epithelial elements exist. Cellular fibro-adenoma possess a morphological structure which may be extremely difficult to differentiate from adenocarcinoma and it is not always easy to state under the microscope whether a tumour is malignant or benign. There is greater realization in recent years of the degree to which cancer cells can assume a spindle shape and it is now known that such an appearance alone does not mean sarcoma. Special methods of staining for reticulum often help to differentiate an anaplastic carcinoma from spindle cell sarcoma.

# Society Proceedings

## Report of the Clinical Conferences

AT THE TATA MEMORIAL HOSPITAL, BOMBAY

Conf on 7 7 44

A case of Malignant Tumour of Bone (?Ewing's) presented by Dr J C Paymaster (†† 7124) A 13 year old boy with a history of fall from a horse 4 months back followed by pain in the upper right thigh of moderate intensity with limping Occasional attacks of fever and loss of weight Inability to move the right hip for the last few weeks On examination a flexion deformity of the right hip joint but other movements of joint free Firm, irregular swelling over front and lateral aspects of upper thigh—tender Extension of hip painful P R—a hard mass arising from pelvic bone on right side X-ray picture showed destructive lesion of pubis and ischium with raising of periosteum Diagnosis primary bone tumour—?Ewing's Enlarged lymph node removed from groin showed chronic lymphadenitis Patient was started on X-ray treatment and after 2 exposures of 150 r each the lad was able to extend his hip without pain and there was appreciable diminution of tumour He had received 1500 r X 2 so far and the tumour had rapidly regressed. In view of the rapid response to X-rays Dr Paymaster suggested that the provisional diagnosis of Ewing's tumour was probably correct (An aspiration biopsy done on 10-7-44 revealed malignant cells It was not possible to classify the tumour The patient was discharged walking and free from pain on 27-7-44 Well so far

Three cases of Ewing's Tumour of Bone were presented by Dr E J Borges (1) †† 7361 A 24 year old male with a 6 months' history of pain in the left groin He noticed a vague swelling in the same area about 2 years ago and this had gradually increased in size There was no pain until 6 months ago No trauma at any time Feverish feeling occasionally Limping for 3 months Examination showed an indefinite swelling over the superior ramus of left pubis involving the femoroperineal groove P.R—a swelling in the left side of the pelvis fixed to the pubic body and inferior ramus X-ray picture revealed a destructive lesion of the pubic bone with a soft tissue mass No periosteal reactions or new bone formation A provisional diagnosis of Ewing's tumour was made He was given deep X-rays and after the first exposure the pain disappeared and the movement of the thigh became less painful (2) †† 5452 A 12 year old girl was brought in October, 1943 with a history of a fall 5 months back without any injury noticed at that time A month later developed painful swelling over upper part of right thigh No fever On examination a bony swelling over upper part 1/2 of right thigh all round Flexion deformity 25° and abduction deformity 25° Rotation free and painless No bony tenderness Skiagram revealed a typical picture of Ewing's tumour with onion peel appearance etc Aspiration biopsy confirmed the diagnosis

She was started on X-ray treatment. After 6 exposures there was visible regression of tumour and cessation of pain and she rapidly improved and was discharged from hospital on 27-11-43 with no limp and no pain. X-ray pictures taken in December, 1943 and January, 1944 revealed marked sclerosis of affected bone. She keeps well. In March, 1944 a routine follow up chest screening revealed a metastatic deposit in the left hilar region of the lung. This was treated with X-rays and disappeared, but 3 weeks later she developed lumps on the skull and protrusion of the right eyeball from orbital metastasis. This latter was treated and the eyeball returned to normal. The other skull metastasis have increased to an enormous size (3) †† 5814. A boy of 16 years with a history of having had a lump in the right pectoral region removed 3 years before with recurrence at the same spot 9 months later. Gradually increased in size until present size of 6" X 4½". Hard tumour fixed to the chest wall. Skiagram showed a soft tissue mass outside and inside the chest with a slight erosion and expansion of part of one rib. Biopsy showed an Ewing's tumour. X-ray treatment produced rapid regression of the mass.

Dr Borges said that he would like to point out certain features presented by the cases of Ewing's tumour seen at this hospital. First the rather prolonged history in two of the cases—2 years' swelling in one and removal of the lump 3 years before in the other. One must therefore remember that a prolonged history does not necessarily go against the possibility of Ewing's tumour. Secondly it was very striking that out of the 12 cases of Ewing's tumour seen at this hospital (all but one histologically proved) there were 3 cases in the pelvis. Thirdly in only one of the cases presented that day and only in 2 of the whole series of 12 was there fever of the type usually described which confuses Ewing's tumour with osteomyelitis. Finally he would like to ask the radiologists if there was any connection between the radiation given to the lung metastasis in †† 5452 and the sudden appearance and rapid growth of the cranial lumps almost immediately afterwards.

Dr L. H. Athle demonstrated the X-ray pictures of the cases presented and discussed their features. He particularly stressed the fact that in only one of the whole series of 12 cases at our hospital was there the characteristic of onion appearance described in books. All these cases had been correctly diagnosed by radiological examination. In the flat bone like the os pubis or clavicle the typical appearances were missing but the diagnosis of primary malignant tumour of bone was difficult to establish, but once that is done, Ewing's tumour would suggest itself by the soft tissue invasion and lack of bone reaction usual to osteogenic sarcoma. Dr K. P. Mody referred to the therapeutic test of radiation on these tumours. He said that there was no relation on these tumours. He said that there was no relation between X-ray therapy of the primary and appearance of metastases.

A case of carcinoma of the stomach was presented by Dr D. J. Jussawalla (†† 6978). A 53 year old man with epigastric pain com-

ing on 2 hours after meals for the last 6 months, loss of weight, appetite good. A fairly well preserved man with a vague suggestion of a mass in the epigastrium. Radiological examination revealed a typical carcinoma of the stomach involving the distal 2/3rds. Exploratory laparotomy showed an inoperable cancer with infiltration of whole lesser omentum. Although adenocarcinoma of the stomach is not a radiosensitive tumour, experimental treatment with deep X-rays as a palliative measure was tried—2400 r. There was considerable relief from pain and the patient felt better. Dr Jussawalla said that more radiation would be dangerous because of the possibility of dissolving the tumour and leaving a perforation in the stomach. A subsequent X-ray examination showed that the tumour was as big as ever, and that X-ray treatment did not have any definite effect on the tumour but certainly made the man comfortable. Dr Athle said the treatment of carcinoma of the stomach by radiation was not a useful procedure except in the highly anaplastic carcinomas and lymphosarcoma of the stomach. He had not seen encouraging results himself.

A case of Lymphadenoid Goitre was demonstrated by Dr D J Jussawalla (†† 7331). A 35 year old male with a large mass in the neck. 2 years ago it started as a small lump in the posterior triangle on the left side and gradually increased in size and extended to the front of the neck. The huge mass caused dyspnoea and hoarseness of the voice. BMR 18 (Mayo Clinic). The mass appeared to be a multilocular cystic tumour in connection with aberrant thyroid tissue. An operation was decided upon but because of the dyspnoea and reslessness of the patient no anaesthetic could be administered. Tracheotomy was out of question as the huge mass completely obscured the trachea. Only a biopsy under local anaesthesia was done, and it was reported as lymphadenoid goitre. Palliative X ray treatment was tried but no appreciable change was noted after 2400 r. This was expected as lymphadenoid goitre does not respond well to X-ray treatment and therefore this was quite in keeping with the pathological diagnosis.

Dr Jussawalla mentioned that lymphadenoid goitres of this size had never been described elsewhere to his knowledge, and that the subsequent progress of the disease would make an interesting observation in this patient.

*Conf on 14 7 44*

A case of Squamous Carcinoma of the Skin of the Hand presented by Dr J C Paymaster (†† 7267). A woman 56 years of age gave a history of ulcer on the medial aspect of the hand on the hypothenar eminence. She had suffered from eczema of the palms and dorsum of the hand for 15 years. Careful interrogation brought out the fact that she had received several X-ray treatments about 12 years ago. Dr K. P. Mody said that the case presented all the features of radiation cancer and cited experiments done at the Royal Cancer Hospital, London, which show that radiation and chronic irritation together may lead to the formation of growths on the skin.

**Dr L H Athle** described the typical changes in the nails, dryness, atrophy and pigmentation of the skin along with patches of hyperkeratosis all over. These changes were localised to the hands. The occupation of the patient was such that she was not exposed to physical or chemical agents known to have a carcinogenic effect. She had no arsenical dermatitis and she was not suffering from Bowen's disease or eroderma pigmentosum. This excluded all the precancerous dermatosis. The changes seen were identical with those seen on the hands of radiologists and surgeons exposed to radiation. **Dr V R Khanolkar** stressed the fact that Basal cell carcinoma had not been described as developing on the basis of radiation dermatitis. The lesion is always of the squamous type. **Dr Meher-Homji** referred to his patient (†† 6121) who was a baker by profession. This man had multiple keratosis all over the body especially on the exposed parts. He had several lesions of squamous carcinoma on his hands and face.

The treatment was then discussed and it was agreed that X-radiation was the method of choice. **Dr Athle** pointed out that these lesions were caused by small doses of radiation repeated over a long period and were curable by a short intensive course of radiotherapy like other skin cancers not caused by radiation. This case was subsequently treated by low voltage therapy with complete disappearance of the cancer.

**Dr E J Borges** showed a case of Juvenile Fibroma of the Nasopharynx (†† 3537). A woman 28 years of age. The large mass had regressed completely under X-ray treatment given 1 year ago. She later came back with headache and 6th nerve palsy due to extension of disease to the base of the skull. This was completely cured and now she returned again with severe headache this time due to a small recurrence in the roof of the nasopharynx. She was undergoing X-ray therapy for this and was improving. **Dr Borges** advocated a conservative treatment of these lesions by radiation followed by careful observation for long periods.

**Dr D Meher-Homji** presented two cases of enlarged supraclavical nodes (†† 7155 & 7161). Clinically these cases appeared to be metastatic in nature. No primary was detected on a thorough search of the probable sites. In one case the aspiration biopsy was positive while the formal biopsy was negative. In the second case a formal biopsy showed chronic inflammation. He felt that in spite of this report and in spite of the unsuccessful search for the primary he was dealing with malignant disease. **Dr V V Gharpure** explained why the aspiration biopsy was positive and the formal negative. He said that the needle had struck the deep lying tumour tissue while the formal biopsy only included the normal superficial tissues over the mass. **Dr Athle** said that this case proved one more advantage of aspiration biopsy and that it was worth trying this method in such obscure problems. He felt that on the strength of the clinical evidence the second case also should be treated as a metastatic malignancy. The benefit of doubt should be given to the patient and not to the lesion. Both the cases were subsequently treated with excellent regression.

**Dr K P Mody** demonstrated a case of a 45 year old male who had complained of constant pain in his throat for 2 years (†† 1615) He was examined in December, 1941 and no disease was detected He was periodically re-examined until August, 1943 when he showed a small granular mass in the right pyriform fossa This was proved to be squamous carcinoma This case brought out several important points, firstly the importance of subjective symptoms, secondly the necessity of repeated examinations and thirdly question of the period during which cancer remaining dormant before it begins to produce symptoms especially the pain noticed in some early cases Dr Athle suggested that pain may be due to the precancerous changes in the submucous tissue and therefore the duration of pain cannot be said to coincident with existence of a fully formed cancer We do not know how long precancerous conditions exist before they assume a truly malignant form Dr Khanolkar dealt at length with the questions of latent precancerous changes and the relations of pain to cancer in the early stages He mentioned that he had been struck with the history of persistent pain localised to a small circumscribed area in some of the early cases which had presented themselves at this hospital and where careful clinical examination had revealed no tumour Several months later in the course of the follow up a tumour was demonstrated in the area related to the sensation of pain A study of innervation of tumours particularly in the early or precancerous stage presented a very promising field of investigation Ludford in London and Boeke at Copenhagen had started a very interesting study of this problem in experimental animals It was proposed to undertake work on innervation of precancerous lesions at this institution, but had to be given up owing to the impossibility of obtaining chemically pure reagents for this purpose during war

*Conf on 21 7 44*

A case of Follicular Lymphoma discussed by **Dr V V Gharpure** (†† 7176) He first gave the clinical history of the case He said that the patient was a Parsee youth aged 20 years He came to the Tata Memorial Hospital for enlarged multiple lymph nodes all over the body He gave history of rhinitis with occasional blocking of the nose since one year In January 1944 the patient had slight fever with cough for 15 days First noticed enlarged nodes in the axillae and consulted a physician who gave him exposures of deep X-ray therapy to both the axillae He found no improvement Patient noticed that more nodes were enlarging One node in the right inguinal region broke through the skin one month back and discharged seropurulent fluid On physical examination it was found that the patient had multiple firm freely movable non-tender nodes in the submaxillary, submental, both axillary and both inguinal regions One node in the right axilla was broken through the skin The edges of the sinus were undermined and pigmented Spleen and liver not palpable Clinical diagnosis was ? tuberculous lymphadenitis and ? Hodgkin's disease Blood studies showed no abnormalities except a positive Kahn test.



A lymph node from left axilla was removed for histological examination and reported as follows (D 626) Gross Description A specimen of a lymph node measuring 4 x 2 x 1.5 cms. Cut surface showed protuberant greyish nodules. Histological examination of the lymph node showed a numerical and dimensional hyperplasia of the lymph follicles. The normal architecture of the lymph node was altered. The lymph follicles showed various sizes and shapes. The germinal centres consisted of three types of cells as described by Symmers<sup>1</sup>. Type one was a large polygonal cell with large pale nucleus, the nuclear membrane was well defined and there were small 1-2 nucleoli. The second type of cell had a nucleus which was denser in chromatin but was a little smaller in size. The third type of cells had richly chromatic nuclei and were much smaller in size and resembled large lymphocytes. In between the follicles was seen a diffuse arrangement of lymphocytic type of cells. The reticulum stain showed that there were practically no reticulum fibrils in the germinal centres. The trabeculae were obscured. Surrounding each follicle the reticulum mesh-work was obviously distorted and condensed by the expanding follicle and the normally loosely arranged network with broad polygonal pulp spaces became compressed and the inter-reticular spaces became markedly elongated and narrowed. Gall and Mallory had stated that such rearrangement of the stroma did not occur in ordinary hyperplasia of lymph nodes and might therefore be considered to be of some diagnostic value. Histological Diagnosis Follicular Lymphoma.

In reviewing the literature on this subject Dr V V Gharpure said that this disease was also known as giant follicular lymphadenopathy or follicular reticulosis. It was first described by Bull, Bachr and Rosenthal in 1925. They called it follicular lymphoblastoma. In the reported cases the average age was 43 years. The course was typically remittent. The average duration of the disease was 4 to 7 years. There might be splenomegaly and there was generalised lymph node enlargement, hypochromic anaemia and effusion into the serous sacs. The enlarged spleen and lymph nodes were radiosensitive.

A recent case of granulosa cell tumour of the ovary was presented by Dr B N Purandare. The patient was 60 years old. Her chief complaint was pain in abdomen for three months. Bleeding per vaginum off and on for the last four years. F M P at the age of 14 years 3-6/30. Menopause at the age of 54 years. L M P began on the 16th January, 1944 and continued till the 31st January, when she was operated. Dr Gharpure then read out the pathological findings of this case. Description of the gross specimen of the ovary (D 98). A specimen of ovarian tumour measuring 13x10x8 cms. The outer surface was smooth and bluish in appearance. The area where it was adherent to the intestine was dark brown in colour. At places it felt cystic and at places it had a solid feel. On cutting into the tumour about 30 cc of mucinous fluid came out. Cut surface showed an area filled with blood clot. No evidence of infiltration of the tumour on

1 Symmers, D: Arch Path. 26, 603, 1938

the outer surface Uterus measured  $4\frac{1}{2} \times 3 \times 3$  cms The uterine wall was 3 cms thick The endometrium was shaggy Blood vessels in the outer part of the uterine wall were prominent Histological examination of the ovarian tumour showed a diffuse arrangement of small polygonal cells The cells had deeply stained, round nuclei containing fine basophilic chromatin granules, there were one to two small indistinct nucleoli The cytoplasm was scanty and faintly basophilic At places the cells were loosely arranged There was no tendency for the cells to be arranged into follicles or trabeculae Diagnosis Granulosa cell tumour of the ovary of the diffuse type Histological examination of the uterus showed a hyperplasia of the uterine glands The glands were tubular and were lined by a single layer of columnar epithelium The nuclei were small ovoid and were situated either at the base or in the centre of the columnar cells The stroma between the glands consisted of small loosely arranged round and ovoid cells Diagnosis Hyperplastic endometrium

Dr Gharpure discussed the significant clinical and pathological features of this case and referred to another case which had a similar clinical history of post-menopausal bleeding (B 944) This patient was 59 years old and diagnosis of the ovarian tumour was thecoma

Dr D R. Meher-Homji suggested that in cases of pelvic neoplasm a uterine curettage should be practised in every case to find out the condition of the uterine mucosa If it was found normal then the pelvic neoplasm alone should be removed Dr B N Purandare wanted to know the distinguishing features between the histology of the uterine mucosa in cases of metropathia haemorrhagica and the proliferated endometrium secondary to a granulosa cell tumour or a thecoma

Dr V V Gharpure replied that in the metropathia there was seen a typical swiss cheese appearance of the uterine glands, thrombosis of the blood vessels and areas of haemorrhage in the stroma In cases of granulosa cell tumour or thecoma the endometrium showed proliferative changes of the glands Dr B N Purandare added that the endometrium showed gross areas of triangular infarction in cases of metropathia haemorrhagica

Dr M V Sirsat discussed the case (†† 2722) of a woman aged 21, who had a radical mastectomy performed on the left side for a lump in the breast on 6-3-37 Subsequently she was operated six times for recurrent lumps in the area of the previous operation at varying intervals She was referred to this hospital on 14-7-42 On examination it was found that there was a scar of radical mastectomy over the left chest and a granulating ulcer situated at the left border of the sternum Supraclavicular nodes were palpable She was given X-ray treatment and by 7-9-42, the supraclavicular node and the ulcer regressed completely She came to this hospital again on 12-11-42 with a recurrent tumour mass which was subjected to cautery excision Patient came to the hospital again on 9-5-43 with a large mass in the abdomen with much pain and tenderness She was operated this time by an outside surgeon and a bilateral ovarian

(Continued on page 388)

# Book Reviews and Notices

**INTRAVENOUS THERAPY** by K V THAKKAR, L. M. & S (Bom U India) Late Chief Medical Officer to the States of Palitana and Idar Second Edition 1944 336 pp. plus 18 pp Index Price Rs 8 8 0 Available from Dr K. V Thakkar, Medical Building Mama Kotha Road, Bhavanagar, Kathiawar, India and from Kothari Book Depot, Parel, Bombay 12

Dr Thakkar deserves congratulations on bringing out the second edition of his book on Intravenous Therapy. This particular method of treatment has made such tremendous strides in recent years that a thorough grasp of its principles and technique is an essential qualification of the efficient physician. Without sound basic knowledge and expert technique, a physician is bound to feel handicapped in the proper discharge of his functions as a modern up-to-date practitioner of the Art of Medicine, and he would welcome any book that would give him the necessary information in a ready and reliable form. Dr Thakkar has amply succeeded in placing before him such information in an easily-accessible manner in his Monograph on Intravenous Therapy. This compilation has further merit of having its usefulness increased by critical reviews of the various methods based upon the author's own personal experience and supported by other valuable critical publications in the medical press. It will thus be clear that the book is a sound and reliable stand-by for all medical practitioners as a ready-reference volume in all emergencies, when one may confidently expect to find the required information in a moment.

This new edition has been brought up-to-date by the incorporation of the latest information about subjects like blood-transfusion and therapeutic agents like penicillin, the sulphonamide-group of drugs including sulphadiazine, and the new anti-plague serum of the Bombay Haffkine Institute, while not omitting the various vitamins.

In our judgment, the book is up-to-date, and thoroughly reliable, and we have no hesitation in strongly recommending it to all medical practitioners. It has been carefully edited, and it is well-bound, clearly printed, and furnished with good illustrations.

S K V

**THE MEDICAL ANNUAL—1944** Bristol, John Wright & Sons Ltd, England pp 404 Price Rs 20

As usual, this is a Year-book of treatment incorporating all the recent advances during the previous year arranged in an alphabetical order for easy reference. In its sixty-second year it needs no further comment to say that it has already established its permanent place in every doctor's library as a reference book. The publishers, in spite of the hardships and the handicaps of the war, have been able to produce a well-bound volume printed on very good paper, and the editors have been at pains to abstract most of the latest publications likely to be useful to practitioners of medicine, surgery, and various specialities. The needs of the general practitioners are kept in mind by the reviewers and the practical aspects of newer treatments are adequately dealt with. Owing to severe paper-rationing, only a limited number of extra copies have been printed, and it is quite possible that if intending purchasers do not place their orders at once, they may have to be disappointed.

S K V

# The Indian Physician

VOL III NO 12

DECEMBER 1944

WHOLE NO 36

## Original Contributions

### STRUCTURAL ABNORMALITIES

#### FOUND DURING DISSECTIONS OF 1456 DEAD BODIES IN SETH G S MEDICAL COLLEGE, BOMBAY

*By*

**Dr G M KURULKAR**

ANATOMY DEPARTMENT

*G S Medical College, Bombay*

From June 1925 to August 1944, the Anatomy Department of the Seth G S Medical College received 2728 dead bodies. Out of these 2728 bodies, 1456 were utilized for dissection purposes. Out of the remaining 1272, 160 were child bodies, 810 being unfit for dissection were macerated, 184 were used for examination purposes and 118 were utilized for operative surgery classes.

Almost all these dead bodies belonged to Hindus. We have never come across a dead body of a Parsee in the dissection hall. Equally rare are the dead bodies belonging to the Muslim or Christian community. This is due to the effective organisation for disposal of dead bodies of these particular communities. Hindus whose unclaimed bodies formed almost all the bulk of our dissection material were mostly belonging to Western India and were of scheduled or Maratha castes. A negligible number (some 10) belonged to Hindus from Northern and Southern India.

Of the 1456 dissected bodies 990 were male and 466 female. Total number of characteristic structural abnormalities found up to date, and collected in the department is 74. Minor variations of structures especially of blood vessels, were not collected. The vascular variations are frequently found in the superior extremities and these have not been recorded. As a routine a student brings to the notice of the staff any irregularity met during dissection. In case any characteristic irregularity is noticed, it is preserved. Pathological abnormalities are not as a routine collected though some structural abnormalities due to pathological processes have been collected, as some special interest seems to be attached in the way these changes had taken place. All the abnormalities we have found are recorded in literature. The

A paper read at the 42nd scientific meeting of the G S Med Coll. and K E M. Hospital Staff Society, Bombay, on Oct. 14, 1944 with Dr R. P. Koppikar in the chair.

classification of these 74 specimens according to different systems is as follows —

	Developmental	Pathological	Total
1 Cardio-vascular system	4	1	5
2 Urinary system	18	8	21
3 Genital system	2	0	2
4 Gastro intestinal system	13	0	13
5 Glandular system	7	0	7
6 Muscular system	1	0	1
7 Bones	9	15	24
	55	19	74

## I Cardio-Vascular System

1 Heart and S shaped aorta	1	Pathological
2 Abnormal right subclavian art.	1	Developmental
3 High division of brachial artery	1	"
4 Abnormal palmar arch	1	"
5 Double inferior vena cava	1	"

Of these five specimens, the specimens of abnormal subclavian artery on the right side, and double inferior venacava, are rare specimens, though they are recorded in the literature

*Abnormal right subclavian artery*—The artery arises from the aorta beyond the origin of the left subclavian artery and proceeds to the right side, going behind the oesophagus This anomaly is due to the disappearance of the fourth right aortic arch completely and persistence of the right arch of the aorta

*Double inferior vena cava*—A rare specimen shows the persistence of supra cardinal veins of both the sides in abdomen

## II Urinary System

The abnormalities here are of three structures (1) Kidneys, (2) Ureters, and (3) Renal vessels

Kidneys —	(a) Horse shoe shaped kidney	4 specimens.
	(b) Pelvic Kidney	2
	(c) Atrophic Kidney	2
Ureters :—	(a) Double Ureters	3
	(b) Fissured Ureters	5
Abnormal Renal Vessels		3

*Horse-shoe shaped kidneys*—In all 4 horse-shoe shaped kidneys were found Horse-shoe shape of the kidney is the result of the union of the lower poles of the kidneys of both the sides Of the 4 specimens, 3 had the typical horse-shoe shape, and one was atypical with a very broad curve

In our series the incidence of the horse-shoe shaped kidney is 0.27 per cent of 1456 dissected bodies In other words 1 in 364 may be expected to have a horse-shoe shaped kidney In Kuester's collection, the percentage is 0.09 per cent or 1 in 1100 The incidence of horse-shoe shaped kidneys in Western India seems to be three times more frequent than in the Kuester's collection

*Pelvic kidney*—Pelvic kidneys were found in two individuals out of 1456 In both these persons, left kidney was found at the level of

the pelvic brim opposite lumbo-sacral joint, forming a lump behind the peritoneum

*Specimen (1)*—This specimen had a normal right kidney at its normal place at the level of the 12D 1L 2L vertebrae Left kidney of this specimen was at the level of lumbo-sacral junction Its renal sinus has a vein and an artery only Ureter starts from the anterior surface of the kidney Artery to the kidney is a branch of the bifurcation of the aorta and veins go to the inferior vena cava An accessory vein arises from the anterior surface

*Specimen (2)*—This specimen has both its kidneys out of place Right kidney is at the level of 3, 4 and 5 lumbar vertebrae Its renal sinus is shallow and extensive going up to the two poles thus giving an appearance to the kidney consisting of two halves, one anterior and the other posterior The renal sinus has the ureter and the vein only There are two renal arteries arising from the aorta passing in front of the inferior vena cava to the posterior half of the kidney at discrete points Renal vein has an unusual ending It passes in front of the inferior vena cava and joins the left border of the vena cava just below the opening of the left supra-renal veins As for this unusual course of the vein it is very difficult to explain

Left kidney is at the level of lumbo-sacral joint Renal sinus receives veins and the ureter Artery goes to the top of the kidney arising from the bifurcation of the aorta and the renal vein goes to the right common iliac vein

Thus both the specimens have left pelvic kidneys These two pelvic kidneys vary regarding the structures going to the renal sinus Right kidney of one specimen is normal and that of the other has not ascended up completely As a result the blood vessels of the non-ascended right kidney are of the interim stage type, 2 in 1456, or one in every 728 is the proportion, percentage is 0.14 per cent of the incidence of pelvic kidney Considering both these anomalies for statistical purposes 1 in every 243 persons may have a horse-shoe shaped or a pelvic kidney, (0.4 per cent) The pelvic type of the kidney seems to be usual on the left side probably due to the migration up of the left kidney later than that of the right kidney

### *Ureters*

*Ureteric anomalies*—These may be classed into two groups (1) Double where both the ureters are opening separately in the bladder, (2) Fissured, when there is only one common opening in the bladder for two ureters arising out of the kidney

*Double ureters*—We have collected three specimens, all of male sex One on the right side and two on the left side The ureters are coming from the renal sinus Statistical analysis shows 1 in 500 or 0.2 per cent being the incidence of double ureters

*Fissured ureters*—There are 5 specimens, 4 male and 1 female Two are of the right side and three of the left side Fissurisation starts from the kidneys and advances up to different lengths from two inches to almost up to bladder

All these specimens except one have two ureters starting from the renal sinus. One specimen has one ureter arising from the sinus and the other from the convex border of the kidney both meeting immediately below the kidney. Thus 1 in 300 individuals or 0.3 per cent will be the incidence of the fissured ureters.

Ureteric anomalies (both double and fissured together) thus would occur in one person in every 182, the percentage being nearly 0.55. According to Kuester, horse-shoe shaped kidney occurs 1 in 1100. In Keen's Surgery the percentage of double ureters (both fissured and double together) is 1 per cent. Ureteric anomalies seem to be mostly common in males, 7 in males and 1 in female of our series. 1 in 141 for males and 1 in 486 in females. More common on the left side (5) than on the right (2).

### III Genital System

Three specimens of undescended testis were collected, out of 990 male bodies dissected. 1 in 330 is the ratio which is higher than mentioned in Keen's Surgery which is 1 in 500. All the three are on the right side.

### IV Gastrointestinal System

*Meckel's diverticulum* was found in 11 bodies. The length ranging from half inch to 2 inches and their blind extremities being free. 1 in 132 individuals is the proportion.

*Duodenal diverticulum*—Only one case of the duodenal diverticulum was come across. Kellogg by barium meals in 6847 persons has found the duodenal diverticulum in 12 per cent of the persons.

*Fetal type of caecum*—Only one instance was recorded.

### V Glandular System

Double levator Glandulae	1 Specimen
Accessory Spleen	4 "
Sequestered Liver	1 "

*Accessory spleens*—The incidence of accessory spleens is reported by Rodney Maingot to be 10 per cent at least. He includes all the discrete accessory spleens, very small minute posterior and big splenic tissue in the gastrosplenic ligament and greater omentum. Our collection is a routine collection and not specially made with an intention of finding accessory spleens. It is natural therefore that we might have ignored small splenic nodules which Rodney mentions. We have 4 accessory spleens, a far too low number in comparison to Rodney.

*Sequestered Liver or Accessory Liver*—We have found one instance of accessory liver at the expense of the left lobe of the liver. The accessory liver is a rounded nodule about 2 inches in diameter, completely covered by the peritoneum attached by a long petritoneum to the porta hepatis (carrying blood vessels to the nodule). This condition is probably due to over atrophy of the left lobe of the liver.

### VI Muscular System

Biceps branchii with three heads of origin, 1 specimen

TABLE

Percentage of Abnormalities to the whole collection of the dissected bodies (1456)					
	G S Medical College Bombay Dissection Hall	Kuester	Keene	Rodney	Kellogg & Radiology
Horse shoe shaped Kidney	0.27% or 1 in 364	0.09% or 1 in 1100			
Pelvic Kidney	0.14% or 1 in 728				
Fissured Ureters	0.8% or 1 in 300	0.55% or 1 in 182	1% or 1 in 100		
Double Ureters	0.2% or 1 in 500				
Undescended Testes	0.3% or 1 in 330 (990 males)		0.2% or 1 in 500		
Accessory Spleens	0.3%		10%		
Duodenal Diverticulum	0.07% or 1 in 1436				1.2%
Meckel's Diverticulum	0.8% or 1 in 132	Standard books on surgery give 2%			

## VII Bones

Developmental abnormalities come across in bones were the following —

- |   |  |             |
|---|--|-------------|
| 1 | Cervical rib fused by the anterior ends with the first rib   | 2 Specimens |
| 2 | A rib with bifid anterior end  | 1           |
| 3 | Two ribs joined by a cross bar of bone in the middle of the shafts   | 1           |
| 4 | A humerus with supracondylar process   | 1           |
| 5 | Clavicle with central foramina   | 2           |
| 6 | A sternum with a central gap in its body   | 1           |
| 7 | Two ribs united completely both at the anterior and posterior ends but separate in the middle of the shaft | 1           |

The rest of the bony abnormalities are due to the non-developmental causes. Out of these two, (1) a pelvis with ligamentous ossification, and (2) a light skeleton, are briefly described below —

## 1 A pelvis with ligamentous ossification

In this pelvis 4th and 5th lumbar vertebrae and sacrum are all fused. Iliolumbar ligaments, fascia covering the sacrospinalis at the back of the sacrum, sacrotuberous and sacrospinous, transverse acetabular ligaments are completely ossified. Sites at origins of gluteus maximus, tensor fascia lata muscles show bony projections. But coccyx is not fused with the sacrum.

## 2 A light skeleton

This skeleton is extremely light, as will be seen from the comparative weights of femur, tibia and fibula of the skeleton and those of normal skeleton of the same size.

	Weight of the normal bones of the same size.	Weight of the bones of the light skeleton	Percent
Femur	320 gms	85 gms	27%
Tibia	157 gms	42 gms	27%
Fibula	28 gms	13 gms.	47%

This skeleton seems to be roughly 1/3 of the weight of the normal skeleton of the same size.



## DISCUSSION

Dr B N Purandare remarked that the genital organs in the human body were the ones, showing the most frequent abnormalities in their development and hence often perplexed the operating gynaecologist. Dr Kurulkar had brought to our notice some of the interesting abnormalities which were likely to trap an operating surgeon. He then stated an instance of a case of caesarean section in which the operating obstetrician not probably realising the anomaly removed a bruised pelvic tumour obstructing the delivery which later turned out to be a kidney on histological examination. About the double ureters Dr Purandare was of the opinion that they were much more frequent than what one would gather from the percentage incidence reported in the dissection hall statistics. He had noted this abnormality on two occasions out of ten cases of Wertheim's operation of cancer of the cervix which needs a thorough pelvic dissection. He then cited a case in which the tube and ovary on each side was contained in a separate sac as is seen in some of the lower species. On the right side this sac had grown in the form of a retroperitoneal cyst and had even lifted up the mesentery on the top of it. Dr Purandare then showed X ray photographs of a case with absence of the lower end of radius and of another new born child with multiple intrauterine fractures. He also showed the actual photographs of a foetus with the deformity of the face resulting from the adhesions with the amniotic membranes and oligohydramnios and another child with absence of the anterior abdominal wall with the abdominal organs exposed and associated ancephaly.

Dr S G Joshi remarked that he had seen a case with two external auditory meati, one in the normal position and the other a little anterior to the pinna. Fluid injected through one opening came out through the other.

Dr R. P. Koppikar in his concluding remarks said that since the inception of the College all the abnormalities as far as possible had been collected though some difficulty was experienced in inducing the students to part with their dissected parts. It was possible to explain most of these abnormalities by a study of comparative anatomy and embryology. He made a strong plea for the dedication of bodies to the dissection hall in furtherance of medical education.

## THERAPEUTIC NOTES

(Continued from p 345)

clean and glistening. Administration of vitamin B complex is a useful adjunct to improvement of diet in treating these patients (L. A. Gregg and F. B. Utley, Pennsylvania, M. J. 46 933, 1943).

**WORK OUTPUT** of trained subjects is decreased following subsistence on diets deficient in vitamin B factors. Persons receiving about one-third of the daily requirement of thiamine and riboflavin soon develop easy fatigue, irritability, lack of pep, anorexia, and increased leg pain during work periods (C. J. Barborka, et al, J.A.M.A. 122 717, 1943).

**CARBOHYDRATE TOLERANCE** in patients with **DIABETES MELLITUS** may be improved by nicotinic acid therapy. On basis of clinical experience with 15 non-diabetics and 12 diabetics the author suggests that nicotinic acid may potentiate the action of pancreatic islet hormone (F. J. Neuwahl, Lancet 2 348, 1943).

**CHANCROID** usually responds satisfactorily to a minimal total dosage of 21 Gm sulfathiazole by mouth in five days, when buboes are present. 29 Gm sulfathiazole given over seven days seems effective. Patients should be observed periodically until lesions are healed (F. C. Combs, et al, Am. J. Syph. Goner. Ven. Dis. 27 700, 1943).

**CONTROL OF THERAPEUTIC MALARIA** is facilitated by use of Thio-Bismol. Optimal time for administration of Thio-Bismol for this purpose is said to be about the fourth day from onset of therapeutic malaria (M. Whelen and P. G. Shute, J. Trop. Med. and Hyg. 46 1, 1943).

Mechanism of action of **VITAMIN A CONCENTRATE IN HYPERTENSION** is obscure. The fact that large doses of vitamin A containing preparations increase urea, insulin, and diodrast clearance of normal dogs suggests that vitamin A concentrates used by the author may alter pathophysiologic pressor mechanism produced by renal artery constriction (G. E. Wakerlin, et al, J.A.M.A. 122 60, 1943).

(Continued on p 344)

# Society Proceedings

## Report of the Clinical Conferences

AT THE TATA MEMORIAL HOSPITAL, BOMBAY

Conf on 11 8 44

### ECTOPIC HYDRONEPHROTIC KIDNEY

Dr E J Borges demonstrated a 20 year old male who complained of recurrent attacks of a painful swelling in the right iliac fossa (†7630) The swelling subsided in 3 to 4 days These attacks had been bothering him for 3 years, once in 3 or 4 months The swelling appeared about 3 months ago but did not disappear as usual It had grown to the size of a melon The swelling was cystic, had well defined contour, fluctuation and thrill were present The clinical diagnosis was a retroperitoneal growth Dr K P Mody discussed the radiograms There was a homogeneous soft tissue shadow in the lower abdomen Barium enema showed pressure from an extra colonic mass Intravenous urography showed absence of excretion on the left side and a normal right pelvic ureter and bladder Ascending pyelography did not succeed on the left side A tumour in connection with the left kidney in an abnormal position was a distinct possibility in his opinion Dr L H. Athle pointed out the peculiar history of the swelling going down spontaneously If this was reliable ectopic kidney with hydronephrosis of an intermittent nature would suggest itself Although the X-ray findings did not directly demonstrate the pathology all the findings were in favour of it Dr A V Baliga discussed the various possibilities from the clinical point of view He said that ectopic kidney or a diverticulum of the bladder could not be ruled out in view of the X-ray findings An exploratory operation was agreed upon but the patient ten days later passed large quantities of urine and the swelling disappeared The patient did not stay for the proposed treatment However, the diagnosis of ectopic hydronephrotic kidney was considered established

### PERFORATED DUODENAL ULCER

Dr D R. Meher-Homji showed a case (†7569) of a perforated duodenal ulcer and described the operative findings Dr Athle discussed the radiograms and showed how the diagnosis of a perforated ulcer was established by the fluoroscopic and radiographic findings prior to operation

### RHINOSCLEROMA

Dr L H. Athle then showed a case (†3484) of Rhinoscleroma involving the nose, lips, palate and pharynx cured by X-ray therapy Photographs taken before and after treatment were circulated The patient was restored to a human appearance by radio-therapy He further described the technique used in these cases

### SARCOMATOUS ADENOPATHY

Dr D J Jussawalla presented a case (†7483) of a 30 year old male who had axillary and pectoral lymphadenopathy In spite of the slight lymph gland enlargement which clinically looked tuberculous in nature, a histological diagnosis of lymphosarcoma was returned in this case The patient was subjected to X-ray therapy and was kept under

observation **Dr Baliga** agreed with the clinical diagnosis and wanted to know if the histological appearances were absolutely indicative of the malignant nature of the lesion **Dr Gharpure** said that they had reviewed the slides but found no reason to consider any other diagnosis

*Conf on 18 8 44*

#### RHINOSPORIDIOSIS OF PAROTID DUCT

**Dr M. V Sirsat** presented notes of a tumour (D 894) of the parotid gland in a girl aged 15 years She was admitted to an outside hospital under **Dr C P V Menon** for a cystic swelling inside left cheek near the opening of Stenson's Duct Duration 4 years The swelling used gradually to increase in size and get bigger while eating her food The girl had to squeeze out the watery contents before she could proceed with her meal The operated material was sent to **Dr V R Khanolkar** for his opinion It was found to be a case of Rhinosporidiosis of the Stenson's Duct Rhinosporidiosis affects primarily the nose, nasopharynx, conjunctivae and lacrymal sac **Dhayagude** reported in 1941 two cases of rhinosporidiosis from two uncommon sites, one from the mucous membrane of the urethra and other a generalised infection all over the body In a review of 45 cases seen by him during 10 years and in a series of 104 cases reported by **Karunaratne** not a single case of rhinosporidiosis of the parotid gland has been reported **Dr Sirsat** mentioned that from the available literature it appears that rhinosporidiosis is resistant to X-ray treatment and even after extirpation it shows a tendency to recurrence **Dr K. P Mody** said, the spores of rhinosporidiosis are very resistant to X-ray treatment and therefore X-rays have no place in the therapy of that condition **Dr A. V Baliga** mentioned a case of a medical practitioner who has been long suffering from rhinosporidiosis of the nose Repeated extirpations have given rise to recurrences

#### THERAPEUTIC NOTES

*(Continued from p 342)*

**ANTITHIAMINE FACTOR** is present in viscera, heads, skin and scales of certain fish When portions of fish containing significant amounts of antithiamine factor make intimate contact with thiamine-containing constituents of the diet, vitamin B<sub>1</sub> content of these foods may be lowered significantly (**P S Owen** and **J W Ferrbee**, New England J Med 229 435, 1943)

**CENTRAL NERVOUS SYSTEM** functional activity becomes abnormal in thiamine and nicotinic acid deficiencies Lack of either or both may result in altered behaviour, ranging from neurotic-like pictures with anxiety to clear cut psychoses In such conditions, nicotinic acid and thiamine therapy may be specific (**M Rosenbaum** and **J Bradley**, M Clin North America 27 431, 1943)

**SENSITIVITY TO SULFAPYRIDINE** appeared to be favourably influenced in a pneumonia patient by administration of 50 mg ascorbic acid Complete disappearance of allergic manifestations ensued within eighteen hours (**J H Schropp**, Canad MAJ 49 515, 1943)

**WHOLE LIVER EXTRACT** apparently reduces **TOXICITY** of diethylstilbestrol and sulfanilamide (Current Comment, J.A.M.A 122 812, 1943)

# Critical Notes and Abstracts

## NUTRITION IN TROPICAL CLIMATES

Dietary requirements are qualitatively similar in hot and in temperate climates. However, they are quantitatively altered in hot climates by increased loss of sweat, anorexia which is very common, and possibly by specific increases in requirements incident to exposure to heat.

R. E. Johnson (*Gastroenterol* 1 832, 1943) points out that water deficiency, resulting in exhaustion and dehydration, can be one of the most rapidly induced of all deficiency syndromes, and may have deleterious effects in only a few hours. Best performance is obtained when men are well hydrated at all times during work.

Deficiency of sodium chloride does not produce heat cramps in a single day even under severe conditions. Hence, replacement, hour by hour is not essential, but replacement day by day in the meals is very desirable. Fifteen to twenty grams of sodium chloride a day appears to be adequate for a large majority of working men.

Within very wide limits, protein intake appears to have little effect upon the well-being or performance of working men. High protein intake has no deleterious effect upon performance in heat. Likewise, low protein intake has no measurable deleterious effects in periods of two months.

Early reports of considerable loss of water-soluble vitamins in sweat, notably thiamine and ascorbic acid, are not corroborated by recent work. It appears that even under the most severe conditions there is a much greater loss of vitamins in the urine than in the sweat.

Maintenance of caloric balance, essential in the long run, is not necessary from day to day. Indeed, very good performance is seen in men whose intake is only one-half the daily caloric output over a period of a week.

## THERAPEUTIC NOTES

**ACTIVE SPRUE** is characterized by failure of absorption which manifests itself in lack of elevation in blood lipids and vitamin A in serum after ingestion of a standard dose of butter fat or vitamin A. Interestingly, during remission, fairly satisfactory fat and vitamin A absorption are encountered (D. Adlersberg & H. Sobotka, *Gastroenterol* 1 357, 1943).

**ASTHMATIC PAROXYSMS** may be relieved by administration of nicotinic acid. Results obtained in a relatively small number of cases indicate that such therapy is valuable in this condition, at present it should be regarded as an adjuvant to accepted methods of management (G. Melton, *Brit M J* 1 600, 1943).

**DISEASES OF THE GASTROINTESTINAL TRACT** are not infrequently associated with deficiency of water-soluble vitamins, including vitamin C. Frequency of vitamin C sub-nutrition in patients

with diseases of the stomach and intestine is attributed to dietary inadequacy (W Bloch, *Z Vitamin f* 13 111, 1943)

**FAILURE** of army drivers to pass the night glare test has been remedied by giving 50,000 units of vitamin A daily for twenty-four days. Importance of frequent testing of drivers for night blindness is emphasized (H J Hutter and E, J Dieter, *Mil Surgeon* 93 31, 1943)

**P VIVAX PARASITES** which are half-grown are markedly inhibited by Thio-Bismol. For termination of P Vivax induced malaria, injection of 0.1 or 0.2 Gm. Thio-Bismol given the day quinine therapy is started usually reacts quicker than quinine alone by preventing a paroxysm the following day (M D Young, et al, *J.A.M.A* 122 492, 1943)

**RECURRENT RHEUMATIC FEVER** often may be prevented by giving sulfanilamide in small doses over long periods of time. Of 16 rheumatic fever patients so treated, there was only one recurrence of rheumatic fever, in a comparable group of 17 patients not receiving sulfanilamide, there were 5 recurrences (C A. Chandler and H B Taussig, *Bull Johns Hopkins Hosp* 72 42, 1943)

**RENAL DAMAGE** and **URINARY TRACT OBSTRUCTION** consequent to precipitation of sulfadiazine and acetylsulfadiazine are preventable. Adjuvant alkali therapy, sufficient to maintain the urine neutral or slightly alkaline, should be prescribed whenever sulfadiazine is given (D R Gilligan, et al, *J.A.M.A* 122 1160, 1943)

**SEVERE EPILEPSY** in 16 cases was definitely modified or markedly improved by treatment with Dilantin Sodium and phenobarbital (D Goldman, *Am J.M.Sc* 205 388, 1943)

**ACNE** in young men responded favourably to sunlight irradiation, supplemented by bi-weekly injections of Antuitrin-S (E J Crisp, *Proc Roy Soc Med* 36 450, 1943)

**HABITUAL VOMITING** may be relieved following nicotinic acid therapy. The authors report several illustrative case histories of habitual vomiting favourably influenced by nicotinic acid in doses of 50 to 75 mg (J G Virasoro and R Monsoliu, *La prensa médica argentina* 30 292, 1943)

**HERPES ZOSTER** has been reported to occur as a complication of treatment with large doses of vitamin B<sub>1</sub>. This is said to provide vitamin B<sub>1</sub> which may have a selective action on the dorsal root ganglions and that, in properly regulated dosage, it may be of therapeutic usefulness in treatment of herpes zoster (P C Baird, Jr, *New England J Med* 22 8568, 1943)

In **PNEUMONIA**, vitamin A, carotene, and total lipid in the blood serum are reduced, reduction follows no regular pattern except that the longer the duration of the disease, the fewer the values that approach normal. Of the 3 factors considered, vitamin A is most rapidly reduced (H W Joseph, *Am J Dis Child* 65 712, 1943)

**TONGUE LESIONS** frequently indicate nutritional diseases. Characteristic feature of nutritional glossitis is thinning of epithelial tufts of the lingual papillae, causing the tongue to seem abnormally

(Continued on p 242 & 344)

# Book Reviews and Notices

**RECENT ADVANCES IN THERAPEUTICS** by J R Goyal M.B. B.S., Second Edition 1944, pp 848 Index Price Rs 6-8-0 Published by the Author Mission Church Road, New Delhi To be obtained from The Medical Review of Reviews P O Box 160, DELHI

The first edition of this review of recent advances in medicine appeared in 1941. In this second edition the author has incorporated the information regarding the clinical use of new drugs such as heparin, penicillin, demerol, octofollin, and has dealt with the sulphonamide compounds more elaborately and extensively than before. The book is divided into two parts. The first contains nine chapters dealing with some eleven (5 common and 6 uncommon) sulphonamide compounds, and the second, contains 20 short chapters dealing with vitamins, hormones, penicillin, heparin, diltantin, prostigmine, aminophyllin, dicoumarin, etc and newer aspects of the treatment of wounds, fractures, shock, burns, schizophrenia, diabetes, epilepsy, syphilis, scabies, etc. The last chapter gives a number of therapeutics tips likely to prove useful to general practitioners. No attempt is made to be exhaustive, or academic, but the information collected from current literature is brief, well presented, and practical. We recommend this review to general practitioners as a handy reliable guide in daily practice.

**INFORMATION REGARDING THE SULPHONAMIDE GROUP OF DRUGS:** Their indications, dosage, etc., (Govt. Press, Bombay)

One of the evils which the new Surgeon-General with the Government of Bombay noticed on his arrival, was the "ignorance of use of the new sulphonamide drugs" among the S M S officers of the province. To dispel this ignorance, this pamphlet of about 4 pages was prepared and circulated to all these officers. It is not for sale but one of our readers has sent us a copy for comments. On the first page there are about 14 rules (numbered by us) or short paragraphs under the heading, "Routine Precautions &c," dogmatically stated and containing no explanations or reasons, and are therefore, we believe, likely to be of little use to the "ignorant S M S Officers". For example, what can they make out of the following? (1) "Patient should be under observation for the first 24-48 hours, and during the course of treatment." What is the longer period of observation? (2) "There may be idiosyncrasy even to small doses" (5) "A routine urine and fluid administration chart should be provided. At least 4 pints of fluids should be given." When? The "ignorant" officer is not told the reason for this precaution, but far down under (13) The officers in the mofussil towns are impressed with the necessity of a resort to "ureteral catheterisation in the first instance, followed by surgical attempts to dislodge the block" in the ureters, without telling them the nature of the block, and can they remove it? Similarly, they are not told what they should expect from (6) "frequent total W.B.C counts." Rule (4) is now obsolete and therefore wrong and the state-

ment under (3) is only partially true, and it is not stated whether the resistance develops in the patient or in the bacteria. Probably in the latter. In that case, as the M R C Memorandum says "a more active drug like sulphathiazole, still exerts some anti-bacterial action when less active compounds have proved ineffective." No precautions to prevent the development of resistance in the bacteria, or of sensitiveness in the patients are mentioned. Rule (7) is irrelevant, as it has nothing to do with the sulphonamides. Under (8) the common toxic reactions ought to have been mentioned. We fail to understand what is meant by "so also in conjunctivitis or dermatitis." Are these drugs to be used locally in the treatment of conjunctivitis (such as the one due Morax's Bacillus etc.) or in pyodermic conditions, or not? We do not at all understand what is meant by (10) "Any drug can be given with sulphathiazole." In the unconscious patients why is there no injection recommended instead of, or in addition to (11) the "nasal" route? Subcutaneous administration is recommended (12) when high blood concentration is desired, but the M R C Memorandum says "Subcutaneous administration may be adopted when there is no need to raise the blood level rapidly."

The table that follows includes 8 compounds, but the last 4 have no relation to the various columns of the table, and should have been dealt with in separate paragraphs. We do not wish to go further into details, for what we have stated above is sufficient to show that the pamphlet is not likely to serve as a guide to the S M S O's, but on the contrary, is confusing, inaccurate and even misleading. Whatever money is spent on its preparation is worse than wasted. It could have been more usefully spent in buying for circulation 100 or more copies of the M R C's War Memorandum No. 10, a booklet of 46 pages, priced 9d. written by a group of experts for the same purpose as intended by the Surgeon-General, who ought to know its existence. Even a summary of it, such as that published in the Clin JI of Nov-Dec 1943 or its review in the Editorial of the B M J of August 14, 1943, would have been far more useful to the S M S O's. The pamphlet is an insult to the education and intelligence of the S M S O's who are now eligible for commission in the I A M. C.

## Announcement

The Indo-Pharma Pharmaceutical Works, Bombay, have reduced the price of their SULPHINDON (U.S.A.—imported Sulphadiazine) to Rs 3/12/- per bottle of 30 tablets. Sulphadiazine is known to be the least toxic Sulpha drug and the drug of choice for systemic Sulpha therapy.

+ + +

Ciba (India) Ltd, Bombay, inform us that they have reduced the price of their well-known Sulphonamide derivative Cibazole (Sulphathiazole) from the 1st January 1945 (20 tablets at Rs 3-5-0 powder 20 grms at Rs 2-4-0 and ointment jars 40 grms at Rs 2-15-0). Any further particulars in this connection can be had from them.

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# THE INDIAN PHYSICIAN

*A MONTHLY JOURNAL OF CLINICAL MEDICINE*

*EDITOR*

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VOLUME IV 1945

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VOL IV NO 1

JANUARY 1945

WHOLE NO 37

## Original Contributions

### IMMUNO-THERAPY IN TUBERCULOSIS

by

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One of the oldest theories of cure, far older than Ehrlich's, was that remedies stimulate the resistance of the body cells in general and so help them to overcome infection. A recent and more definite version of the resistance theory, however, is that the products of infection serve as stimuli to the body cells calling forth renewed cellular activity with production of various specific weapons "the antibodies" which maintain an incessant struggle against the invading pathogenic agents in an effort to rid the body of them and to neutralize their baneful influences. Recent experience with specific chemotherapy has not altered the position in any way and even today the immune bodies occupy the same important status in the fight against the disease as they did centuries ago. Thus in the case of our most potent chemotherapeutic agent (quinine) in malaria, it has definitely been established that the concentration of quinine in the blood attained after appropriate therapeutic doses, is not sufficient to kill the protozoa by direct action in vitro but some other factors also come into play to effect cure. It has been suggested that possibly an antigen from the destroyed parasite stimulates immune body production and helps to overcome the infection.

Again in the realm of acute bacterial infections like pneumonia, Anderson (1943), while assaying the value of sulphapyridine concludes that the mortality rate of lobar pneumonia has not been materially affected by the exhibition of this drug in persons over the age of 40 and suggests that probably the tissue resistance (which of course gradually wears off with advancing years) is an essential adjuvant to chemo-therapy.

Lastly the virus diseases are in no way exception to this and the employment of convalescent sera both for prophylactic and thera-



peutic reasons in majority of these diseases, lends support to the view that the antibodies play the same important role in this sub-group of diseases

With such data at our disposal, is it too much asking oneself why tuberculosis should behave differently? Moreover the failure of infection to manifest itself clinically in majority of the population under the same circumstances and also the varied response on the part of the host to tuberculo-toxin, culminating in one case in acute pneumonic tuberculosis while in other in chronic fibroid type, indicates that perhaps the tissue resistance is of far greater importance in Koch's infection than in any other case

As a result of extensive investigations there are strong reasons to suppose, though some doubt it, that the resistance of susceptible animals such as man, rabbits, guineapigs, etc., to tuberculosis can be increased by infection with either virulent or avirulent human or bovine strains and also to a moderate extent by the injection of suspension of killed tubercle bacilli. Numerous anatomical studies of primary and reinfection types of tuberculosis offer abundant evidence that partial immunity results from the infection with the tubercle bacillus. The primary or childhood type of tuberculosis occurs when the organisms lodge in the body that is neither allergic nor immune and in such cases the original lesions may be anywhere in the lung, no allergic symptoms are detectable and the regional lymph glands soon become involved. In the re-infection or so called "adult type" of pulmonary tuberculosis the lesion is as a rule in the apex of one or both lungs, allergic symptoms may develop and the regional lymph glands are not involved because the tissue immunity due to the first infection localizes the organisms and limits the pathway of spread largely to the bronchi.

In this connection it is of interest to mention some observations of Kayne (1943). The lowest degree of natural resistance will not, on first contact with the bacillus, prevent an extensive primary complex with rapid generalisation and death. A higher degree of natural resistance will lead to primary complex with perhaps some dissemination and recovery but no acquired resistance will follow, so that a fresh infection under bad environmental conditions will again result in a primary complex, this time with generalisation and death. A still higher degree of natural resistance will cause a primary complex, recovery from which will give acquired resistance, and therefore any subsequent re-infection will not produce a primary complex but parenchymatous lesion which tends to liquefy, cavitate and spread by the bronchi.

With all this, it must be confessed at the same time that in spite of the wide distribution of the disease we have little knowledge of the actual mechanism and the nature of the resistance. That antibodies are formed is certain, as is shown by the phenomena of phagocytosis, opsonin formation, agglutination and complement fixation, but we are ignorant of the exact part played by such bodies in overcoming the infection.

Further it has been found that antigenically, Koch's bacillus like many other organisms exhibits type specific and group reactions with regard to antibody formation in susceptible animals but the isolation of such antigens has still been a mystery

Various attempts have been made from time to time to take the fullest advantage of these immunological problems in the treatment of tuberculosis, the introduction of tuberculin being the first step in this direction, the remedy being hailed as a specific weapon, unfortunately to be soon discarded due to inconstancy of results and difficulties of its exhibition. Later on anto-toxic sera were used for the treatment of tuberculosis. Mergliano (1889) prepared such serum which was found to be very useful by Mircoli. Marmorek (1903) claimed good results with this anti-toxic serum in pulmonary tuberculosis and tubercular pleurisy. The serum was tried by a large number of observers with divergent results. Thus Ullman spoke of the serum as a specific remedy superior to all other methods of treatment and Monod, Baer, Schenker, and Roever, to quote only a few, were favourably impressed with its value. On the other hand Krause and Mann found the serum to be useless in cases of pulmonary tuberculosis.

Spengler (1908) prepared 'I.K.' (Immune Korper) from the red blood corpuscles of immunised animals but was subsequently found to be useless by various workers.

"Contratoxin" prepared by Mehnarto was supposed to be specific but met with the same fate.

Antistreptococcal serum was employed on the plea that much of destruction of pulmonary tissue in cases of phthisis is due to secondary infection of ulcerated surfaces by pyogenic bacteria, especially streptococci, and the results reported have been favourable.

However, the advent of collapse therapy inflicted a decisive blow to further efforts at the elucidation and isolation of specific antibody and we really doubt the justification of this lack of interest in a problem which has not materially lost its importance in our fight against tuberculosis merely because a very small percentage of cases benefit from collapse therapy. The object of this paper is merely to stress the need for further investigation on the possibility of raising the resistance of tubercular patients by the use of specific immune body.

Naegell's famous post-mortem survey in 1900 showed that about 98 per cent of the population over 18 were infected with tuberculosis but that only a small percentage of these died of the disease. Again as a result of autopsy examinations, Ople (1917) reports evidence of tubercular infection in 100 per cent of those dying above the ages of 18 showing thereby that an average adult particularly in the cities does become a victim to Koch's infection at one time or other of his life and thus carries in his blood antibodies concerned in the control of tuberculosis. Numerous tuberculin surveys carried all over the world further lend ample support to the so called "Ubiquitous Nature" of the infection. Taking advantage of these observations we have recently tried the crude method of introducing these anti-bodies in whole blood to supplement other modern methods of treatment of

pulmonary tuberculosis and found it to be a measure of distinct value. Donors selected were healthy, dark skinned persons of 35 or more. Preliminary blood examinations and Wassermann tests were carried out to exclude malaria and syphilis and the Montoux test was also performed to establish previous infection. Highly positives were however rejected for fear of allergy. It was further found that those conforming to Bouchard's Arthritic Diathesis—broad, stocky, heavy set, with decreased metabolic processes, highly concentrated food intake and diminished output were particularly suitable. (The arthritic diathesis described by Bouchard was originally considered as incompatible with tuberculosis, individuals belonging to this constitutional entity while they may develop tuberculosis, have some apparent resistance to disease even in the presence of tuberculosis infection). Citrated whole blood was used, the amount varying from 250 cc—400 cc at each sitting and the transfusions were repeated at more than weekly intervals. In our series of cases we have not come across any serious reactions except rigors and rise of temperature to 102-103° F during the following 24 hours in a few cases. Urticaria was, however, noted in one case. Alkalies and plenty of fruit juices and fluids were given to the patients after transfusion.

#### DISCUSSION

The beneficial effect of a therapeutic agent is due to either its being bactericidal or bacteriostatic or its power to neutralise toxins of the invading pathogenic organisms. In other cases, the defensive mechanism may be stimulated in a specific way to check or overcome infection through the medium of a specific immune body. In spite of the vast amount of work the hope of finding an agent, which would penetrate the avascular tubercle, the phagocytic cells containing Koch's bacilli and the bacilli themselves, has not materialised as yet but it is possible to visualise an indirect attack on Koch's bacillus through the medium of a potent immune body. Unfortunately, the present immunological problem of tuberculosis has not been worked out and it is aptly said (Kayne 1943), that it is just like entering inadequately equipped territory much explored yet little chartered. Anyhow, without entering into the controversy as to how the infection fails to end clinically in disease in a particular person, it would appear pertinent to suppose that there must be some exhibition of the defensive mechanism stimulated specifically either by Koch's bacillus or its products of disintegration during its sojourn in the human body.

For purposes of specific treatment two forms of the disease may be distinguished

- 1 *Acute non-pulmonary tuberculosis*—There is an acute toxæmia with symptoms closely resembling those of enteric fever, it indicates an almost complete lack of resistance to the bacilli and is met with in children and young persons. Theoretically, an anti-toxic serum or better still the whole blood from healthy donors would be the only suitable remedy.

**2 Pulmonary Tuberculosis**—In majority of cases who present themselves for treatment, we are probably dealing with more or less localised lesions in the lung with the escape of tuberculo-toxins and perhaps bacilli in some which are responsible for general toxæmia. The clinical status of the patient in pulmonary tuberculosis depends upon the extent of encapsulation of tubercle bacilli, the extent of dissemination of tuberculo-toxin to the adjoining lung parenchyma and the facilities of bronchial spread from the lesion. Thus if somehow or other the organisms could be bottled up at their site so as to limit the escape of toxins which are not only responsible for the down-hill trend of the patient but also pave the way for bacterial spread and further damage, the vexed problem of the treatment in tuberculosis could be solved to a greater extent.

The immune body introduced in the blood of the host, of course in a crude way of whole blood transfusion, could rationally be supposed to counteract the toxins at the site of their elaboration and perhaps cause bacteriostasis and even bacteriolysis and check further damage either to the lung parenchyma or to other body tissues and at the same time give a valuable respite to an overwhelmed defensive mechanism, though temporarily, enabling it to fight a winning battle later on.

We have tried blood transfusion in both types of cases with promising results.

Further, normal human serum is supposed to contain immune bodies against streptococci and other secondary organisms and it would thus appear that its use may provide an added protection against secondary infection. In addition, nutritive value of whole blood is a definite help to the patient.

Lastly, the process has got a great psychological aspect, which in turn is a great asset to the process of recovery.

In the end it must be confessed that the process cannot restore injured tissue cells, but it should be borne in mind in this connection that the army of defence used by the body both in preventing and in combating infection and its sequelae is made up like the nation's defence of many units or factors among which the antibody division can be considered as an important and highly specialised one and this combined with other recognised methods of treatment can go a long way to win the battle.

#### A FEW CASE REPORTS

**No 1** J P, 11 years, male student came under our care as suffering from high fever, marked emaciation, diarrhoea, slight cough. Duration one month—Previously treated as a Typhoid case.

**Examination**—Body reduced to skeleton, tender and distended abdomen, glands palpable more on the right side, temperature 103° 105° F, pulse 140 S R 145 mm, slight enlargement of the cervical glands on both sides, a few rhonchi in the lungs, skiagram revealed basal congestion of the lungs.

**Treatment**—General and pneumo-peritoneum for a fortnight. No improvement decided to give blood transfusion and the child was transfused with whole blood 4 times at weekly intervals, 250 cc of blood being given at each sitting.

Marked improvement after third transfusion. Temperature came down to 99° F and diarrhoea stopped. After 1½ months treatment became afebrile S R normal ambulatory and has reported twice since doing very well.

**No 2** A S 14 years male student suffering from fever 99° 101° F. Duration one month.

**Examination**—Emaciated but a bright face, slight enlargement of glands in the neck. Abdomen distended, painful and tender especially on the right side, frequency of stools, palpable mass in the right iliac region.

Treatment.—General and pneumoperitoneum for 3 weeks without much relief. The patient was then given 3 transfusions of 200 cc of blood at each occasion.

Marked improvement after the second transfusion, temperature came down to normal, started gaining weight and is keeping fit.

No 3 S D, 24 years female, married, primipara, complained of cough, fever, expectoration, haemoptysis and marked weakness.

Examination.—Severe anaemia, marked emaciation, slight oedema of the feet, loose stools, tender and distended abdomen, temperature  $102^{\circ} 104^{\circ} \text{F}$ , Lungs showed coarse crepitations, rhonchi and bronchovascular breathing in upper and middle zones of both lungs. Skidagram revealed extensive bilateral pulmonary lesions, S R 110 m.m. sputum positive—a highly toxic case.

Treatment.—General, Blood transfusion and pneumoperitoneum. The patient was transfused 4 times with 400 cc of whole blood at each sitting.

Marked improvement after 3rd transfusion. The temperature came down, S R. 45 m.m., started gaining weight. She is keeping good health.

No 4 M A, 22 years male, complained of cough, expectoration, fever, loss of appetite, emaciation and haemoptysis. Duration 1 year.

Examination.—Marked emaciation, temperature  $99^{\circ} 103^{\circ} \text{F}$ . Partial artificial pneumothorax on the right side, and also crepitations on the left side. Sputum positive.

Treatment.—General blood transfusion and pneumoperitoneum. As the patient was fairly toxic, he was given 4 transfusions of whole blood of 400 cc at each sitting. The temperature range fell down, gained weight, improved in general health.

No 5 B K, 35 years, married mother of six children, history of pleurisy 4 months back, complained of cough, fever, loss of weight and indigestion.

Examination.—Marked emaciation, temperature  $99^{\circ} 102^{\circ} \text{F}$ . Lungs showed evidence of tuberculosis on both sides—clinically as well as radiologically. Sputum positive.

Treatment.—General blood transfusion, pneumoperitoneum and phrenic avulsion. She was given one transfusion of 300 cc. Showed marked improvement. Temperature came down, was stabilised, started gaining weight (Thoracoplasty performed later on).

No 6 Mrs B, 33 years, complained of fever, cough with expectoration and hoarseness of voice. Duration 15 days.

Examination.—Emaciation, temperature  $97^{\circ} 99^{\circ} \text{F}$ , Pulse 92, Sputum positive, S R 55 m.m. Lungs showed a few scattered crepitations on both sides. Skidagram revealed fine mottling both sides.

Treatment.—General blood transfusion, gold and pneumoperitoneum. She was transfused twice with whole blood 150 cc, at the first sitting while 450 cc at the second.

Marked improvement after the 2nd transfusion, temperature normal, no cough, no expectoration. S R. 35 m.m., No crepitations, skidagram revealed slight improvement of the lesions. Pneumoperitoneum continued.

No 7 A J, 23 years, female, complained of weakness, fever and cough with expectoration. Duration 6 months.

Examination.—Marked emaciation, temperature  $99^{\circ} 101^{\circ} 6^{\circ} \text{F}$ . Pulse 120, sputum positive, weight 70 lbs. Lungs showed bilateral crepitations with bronchial breathing on the left side upper part. Skidagram revealed patchy infiltration all zones more on the left side.

Treatment.—General, left artificial pneumothorax failed, pneumoperitoneum started. In addition the patient was transfused three times with whole blood—400 cc, 450 cc and 450 cc, stationary after third transfusion, sputum positive. S R 50 m.m. Left against medical advice.

No 8 D S, 21 years, Male, complained of fever, cough with expectoration, loss of weight.

Examination.—Temperature  $102-4^{\circ} \text{F}$ . Sputum positive. S R 95 m.m., weight 118 lbs. Lungs showed bilateral crepitations all zones. skidagram revealed tubercular infiltration all zones both sides.

Treatment.—General and pneumoperitoneum carried out for 3 weeks without any improvement, then the patient was transfused with 400 cc of whole blood and pneumoperitoneum was continued. Remained under care for two months. Temperature normal, no cough, no expectoration, sputum positive, weight 139 lbs. S R. 35 m.m., skidagram revealed improvement of the diseased area.

No 9 M, 17 years, female, admitted in the Sanatorium about a year back. Her skidagram revealed patchy tubercular infiltration left upper lobe.

Artificial pneumothorax was continued on the left side for six months, after which she developed fluid. Pneumoperitoneum was then tried and the patient was discharged as much improved. After another six months she began to get fever  $99^{\circ} 100^{\circ} \text{F}$ , loss of weight, cough with expectoration. It was decided to perform thoracoplasty on the left side and as the patient was very weak, 350 cc of blood transfusion was given two days previous to first stage of the operation. After 25 days another 450 cc of blood was given again two days before the second stage of the operation. Then another 550 cc of blood were given after another 10 days. The patient stood the operation quite well, gained weight by 10 lbs. and is now progressing satisfactorily.

N B.—The S R. were all done by Westergren method.

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# PERFORATED PEPTIC ULCER OF THE STOMACH & DUODENUM

BASED ON A STUDY OF 116 CASES

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## INTRODUCTION

I feel that I owe you an apology for the infliction of yet another purely statistical and analytical survey. There is, however, a small justification. It has been generally regarded here that the perforated peptic ulcer, particularly duodenal, enjoys a fairly low mortality rate. This belief has been strengthened by the fact that most surveys from England and America place the overall mortality between 7 and 25 per cent. Apart from the fact that we probably receive a much larger number of late cases and other collateral factors like diet, intestinal flora etc., which affect the mortality rate of our cases adversely, it is my belief that with better preparation of the cases and more vigorous and rational post-operative treatment, our figures could be very much better. As it is, in our present series under discussion, the total mortality rate is as high as 45 per cent, practically 1 out of every 2, a fact which certainly does not leave any room for further complacency.

The cases analysed are those of a consecutive series treated in the KEM Hospital, Bombay, during the last 10 years—i.e., from 1934 onwards and includes cases till May, 1944. Only those that have been definitely established as cases of gastric or duodenal perforation at operation or post-mortem are considered, doubtful cases or those where both operation and post-mortem were refused, have not been included. Also, only acute and sub-acute perforations are listed, chronic perforations being omitted. The total number of cases in this series is 116, of which 93 are duodenal and 23 gastric (including pyloric and pre-pyloric ulcers), a ratio of 4 : 1. There were no cases of perforated secondary gastro-jejunal or jejunal ulcers. Of the gastric perforations one was a doubtful case of ulcer-cancer. 106 cases were operated upon and 43 died after operation, an operative mortality of 40.5 per cent. Total number of deaths, including the cases not operated upon but confirmed by subsequent autopsy, were 53, giving a total mortality of 45 per cent. While certain statistical data will be briefly reviewed, stress will be laid particularly on treatment and mortality factors. As regards the important question of end-results of cases with recovery and their subsequent fate, another apology is due. The absence of any follow-up records and the difficulty in tracing old cases make it impossible for an adequate review of the final end-results. This aspect of the subject has not therefore been considered in this paper.

## INCIDENCE

*Age*—The age-incidence of patients in this series is somewhat different from the western figures. The greatest total number (gastric and duodenal) occurred in the third decade, (44·8 per cent). However, the largest number of gastric perforations occurred in the 4th and 5th decades. Of the perforated duodenal ulcers, 93 cases 47 perforated in the 3rd and 25th in the 4th decade, 50·5 and 26·9 per cent respectively. Of 23 perforated gastric ulcers, 8 occurred in the 4th and 7th in the 5th decades, 34·8 and 30·4 per cent respectively. The other age-incidences are shown in the accompanying chart. Thus we see that there is a definitely earlier age-incidence (by about a decade), of perforated duodenal ulcers as might be expected, for the usual time of onset of duodenal ulcer symptoms is before 30 and gastric ulcer symptoms are infrequent before 40. The youngest patient was 13 years old (acute gastric ulcer) and the oldest 70 (chronic duodenal ulcer). The youngest duodenal case was 15 years old (sub-acute ulcer) and the oldest gastric case 55 (?ulcer-cancer). As opposed to these figures, Estes and Bennett (Bethelhem, Pa) quote the greatest incidence of gastro-duodenal perforation in the 5th decade. In general the figures in the present series appear to be a decade earlier than the American figures of Estes and Bennett, De Bakey and others, probably because of an earlier age-incidence of peptic ulceration in this country. The figures quoted by S. Mohan Rau of Madras General Hospital are fairly similar to those of the present series.

*Sex*—Of the total of 116 cases, 5 were female (4·3 per cent) and 111 male (95·7 per cent), a ratio of one female to 22 males—a much larger percentage than quoted by others—(Estes, 2 females in 80 cases, Rao, 1 female in 106 cases). The incidence of female in perforated gastric ulcers is much higher than in duodenal perforations. Of 23 gastric perforations, 4 were females (17·3 per cent) and 93 duodenal, only one (1·07 per cent).

*Occupation*—The highest number of cases were amongst mill hands, 26 cases. Next in frequency were bus or motor drivers, 7 cases, domestic servants, 6 cases. The rest were all of different callings, mainly drawn from the lower strata of society, workers, labourers and artisans like fitters, electricians, cobblers, etc. Only 5 were brain workers such as teachers, clerks and students (4·5 per cent). There were no physicians or doctors.

While the high incidence of gastro-duodenal perforations amongst the labouring class and low incidence amongst mental workers in this series may be ascribed to the fact that the hospital draws its patients mainly from the poor and the lower middle classes, it is probably more real than apparent. The popular conception that the high-tensioned, hard-working intellectual is more prone to gastro-duodenal ulceration and perforation does not seem to be substantiated by the statistical analysis of other workers as well. A low incidence in brain workers is stressed by most investigators. Thompson in an analysis of 453 cases found that only 19·3 per cent were mental

workers Perforation (6 per cent in this series) among car or bus drivers probably carries a special etiologic significance Shelley also made this interesting observation quoting a 10 per cent incidence amongst car and bus drivers in a series of 82 cases Shawn mentions an incidence of 5.7 per cent in his series, in De Bakey's very large series only 2.4 per cent were chauffeurs

*Community*—The communal incidence was as follows—99 cases were Hindus, 10 Muslims and 7 Christians out of 116 cases

*Seasonal*—According to De Bakey's figures there is a fairly equal division of these cases in the various seasons and no evidence of any definite seasonal variations In the present series, however, a great majority of cases appear to have occurred in winter (or whatever we call winter here) i.e., in the months of November, December, January and February 53 cases, i.e., 45 per cent (nearly half) occurred during this season, the peak being in December (15 cases) During the summer months (March, April, May and June) the incidence was the lowest, 26 cases (20.7 per cent), and in the rains (July, August, September and October) there were 37 (31.9 per cent) cases

*Yearly*—Much has been written about the increased incidence of peptic perforations in cities subjected to aerial bombardment and the activation of gastro-duodenal ulcerations in general, during the present times, with its alterations in dietetic, environmental and emotional conditions Whether it is the result of a total increase in number of patients admitted in the K.E.M. Hospital, or a reflection of the rise in the population of the city or an actual change brought about by the present war conditions, is difficult to decide, but the total figures have been rising steadily since 1938, the peak being in the last two years, 1942 and 1943 (See accompanying chart) A chart of total admissions in this hospital from 1934 onwards (for each year) is also shown here for comparison

#### ETIOLOGY

Sufficient indications were found in the historical data in 67 cases to formulate possible immediate etiologic factors responsible for the perforation They are summarised as under —

1	Relation to food intake (shortly after a meal immediate to within half an hour)	23
2	Premonitory pain (continuous dull crisis like different from the usual type 1 to 7 days duration)	20
3	At work (driving a lorry or car etc. 3 cases)	6
4	During sleep	10
5	Trauma and strain—direct and indirect (one struck in the abdomen with a heavy blunt instrument two, lifting a heavy weight three straining at stool)	6
6	After an alcoholic bout	2
Total		67

It is interesting to note that food-intake seemed to play the largest part In 23 cases where food appeared responsible, acute pain commenced either immediately or within half an hour of the meal The role of lack of food, or an empty stomach could not be assessed as the information regarding time elapsed since the last meal was not available in many cases Pre-monitory, pre-perforative pain in the epigastrium of a continuous aching type, different from the usual intermittent pain of ulcer (duration from 1 to 7 days) was present in the next



largest number, 20 cases. This probably is caused by the involvement of the serosa in the extension of ulcerative process. One case was actually opened up during such a 'crisis' and as no actual perforation was detected, the ulcer area was merely inverted and abdomen closed. Any exacerbation of ulcer pain, therefore, specially if the pain becomes continuous, should be regarded with suspicion. Work, particularly strain during work, was apparently a factor in six, and it is suggestive that three of these six were driving a bus or car at the time—an occupation that involves a great deal of physical and mental strain. As a matter of fact, in this series of 116 cases, there are no less than 7 professional bus or motor drivers. Trauma, both direct and indirect, was responsible for 6 cases. Two cases perforated while lifting a heavy weight and 3 gave a distinct history of onset of symptoms during straining at stool. One came with signs of peritonitis after being struck a severe blow on the abdomen with a hard blunt instrument, laparotomy revealed a perforated chronic duodenal ulcer. As this case had no previous history of epigastric pain, it raises a tricky medico-legal question—"Was the injury responsible for perforation or not?" This man fortunately did not die but in the event of his death the problem would have been very similar to that of rupture of an enlarged spleen on receipt of slighter abdominal trauma. Externally applied trauma is also interesting from the workmen's compensation point of view in cases of injuries sustained at work. Numerous authors have directed attention to the fact that such trauma can be an immediate causative factor in the development of perforation. Different observers from Moynihan onwards have listed the frequency of trauma as a causative factor variously from 2 per cent to 20 per cent. Sirokhine found the incidence approximately 20 per cent in 51 cases. Corlette, on the other hand, studied the problem on the basis of laws of physics and showed that according to an application of Boyle's Law, no increase of general intra-abdominal pressure can cause strain in an ulcer and perforation from such a cause cannot occur. Of further interest is the work of Beams, whose experimental observations show that physical exertion does not increase the tone and motility of the stomach, but often has a contrary effect and renders the organ toneless and flaccid.

While it is obvious that large number of factors are responsible for ultimate production of perforation like tobacco, alcohol, oral and other sepsis, irritants in food etc, the etiological factors discussed above seem to play a fairly direct and immediate part.

#### **PATHOLOGY**

*Type*—Of 116 cases in this series, 93 were duodenal and 23 gastric. There were no gastro-jejunal or jejunal ulcers. There were only 2 proved cases of acute and sub-acute ulcers, 1 duodenal and the other gastric. The rest were all chronic ulcers. One Gastric ulcer was a doubtful case of ulcer-cancer.

*Situation*—Of 93 duodenal ulcers, 89 were situated in the first part of the duodenum, 86 (93.4 per cent) were situated anteriorly and 3 (3.2 per cent) were posterior perforations. Two cases were perforations of the second part, both anterior (11 per cent). In 2 instances

no mention was made of the exact site In the gastric series the situation of perforated ulcers were as follows —

Situation	No of cases	Percentage incidence
Pyloric	5 (Anterior)	21.7 per cent.
Pre pyloric	2 (Anterior)	8.7 "
Lesser curve		
(a) High up near cardia	5 (Ant. 4 Post. 1)	21.7 "
(b) Lower down	9 (Ant. 8 Post. 1)	39 "
Greater curve	1 (Anterior)	4.4 "
Posterior surface	1	4.4 "
Total	28	

The largest number of gastric perforations were on the lesser curve Pyloric ulcers (including 2 Pre-pyloric ulcers) were next in order of frequency—here, an error may have crept in the exact location—for quite often many so-called Pre-pyloric ulcers are truly duodenal, with scarring and fibrosis spreading on to the juxta-pyloric region The ulcers situated high up near the cardia attract our attention since they appear to have a very high mortality rate All 5 such cases in this series died These perforations are also more difficult to repair which adds to the operative mortality The perforation detected on the greater curvature was from a chronic ulcer situated anteriorly Usually it is said that ulcers situated on the greater curve are malignant but the one in this series was an innocent small chronic ulcer

*Number of perforations and ulcers*—In this series there were no instances of double or multiple perforations, though in 3 cases multiple ulcers, duodenal, and gastric+duodenal, were detected

*Type of perforation*—Twenty gastric and 86 duodenal ulcers were definite cases of acute perforation Ten cases, 3 gastric and 7 duodenal, were perforations more of a sub-acute nature

*Size*—The largest gastric perforation found was nearly 3 inches in diameter The largest duodenal perforation was about  $\frac{1}{4}$  inch in diameter

*Bacteriology*—Cultural examination of the peritoneal exudate was carried out in only 2 cases They both showed the presence of Strepto Non-haemolyticus (Faecalis), E Coli, and Staphylococci.

#### SYMPTOMATOLOGY

*History*—About 80 per cent of cases had a history of rapid onset or almost dramatic suddenness There were, however, a fair number of cases which gave a history of exacerbation of previous ulcer pain for a varying period prior to perforation and there were some cases of a sub-acute 'leaking ulcer' type as well, which came on more gradually

*Previous symptom of ulcer (a) —Ulcer pain*, In 69 cases (about 60 per cent) there was a previous history of epigastric pain suggesting an ulcer, which may be summarised as under —

	Duodenal	Gastric	Total
Short history (1 to 6 months)	9	3	12
History of medium duration (6 months to 2 yrs.)	12	3	15
Long history (more than 2 yrs.)	24	0	24
Vague history	7	2	9
Total			60

In the rest a history of previous ulcer pain was not available

(b) *Pre-perforative bleeding*—A definite history of pre-perforative bleeding was present only in one case, where a case of perforated gastric ulcer gave history of haematemesis a month earlier

(c) *Previous perforation*—Two cases in this series were previously operated for another perforation, an incidence of 17 per cent. One was a recurrent duodenal perforation and the other a perforated pyloric ulcer following a duodenal perforation sutured a year earlier

*Symptoms*—*Pain*—Most cases complained of sudden, severe, agonising epigastric pain associated with a catching of breath, with the pain aggravated by any movement including respiratory movements. In fact, I have come to rely considerably on these two features, viz., the sudden onset of epigastric pain together with this characteristic type of catching of breath. In connection with the site of pain I have often employed, and found very useful in diagnosis (specially in perforated duodenal ulcer), a test which one might call a 'pointing sign' for peptic perforations. If the patient is asked to point with one finger and show the exact spot where the pain started, he usually places the tip of the finger just below xiphoid cartilage. Though I am not able to say in what exact percentage of cases this sign is positive, it was present in the majority of cases I have seen, specially perforated duodenal ulcers. Of the 116 cases, 41 also complained of pain and were tender and rigid in the right iliac fossa (35.3 per cent). One case which deserves special mention, complained of pain in the right iliac fossa and was operated first through a McBurney's and when the appendix was found normal, a regular laparotomy was done and a duodenal perforation was discovered. This error is almost classical. Generalised pain was present only in the late cases. Pain in the right shoulder was mentioned only in 3 cases (2.6 per cent) though I believe the incidence is greater.

*Vomiting* was present in 93 cases (79.3 per cent). An odd and fairly early symptom present in 8 cases (6.8 per cent) was difficulty in passing urine or actual retention probably caused by spasm induced by the gravitation of irritating acid gastric juice to the Douglas' pouch.

*Clinical Picture*—Rigidity and tenderness were present in practically all the cases. Rigidity was absent in 3 late cases (2.5 per cent) of over 48 hours' duration. Free fluid was present in 55 cases (47.4 per cent). Free gas, as evidenced by obliteration of liver dullness was present in 72 (62 per cent). Both free gas and free fluid were present in 40 cases (34.6 per cent). Intestinal sounds were absent in 59 cases (50.8 per cent) and the classical triad of perforation, —free fluid, free gas, and absent intestinal sounds were present in only 37 cases (31.8 per cent). It is of note that obliteration of liver dullness was present in as many as 72 cases (62 per cent). Its diagnostic value, however, is open to doubt. Apart from other causes of diminished liver dullness, such as gaseous distension of the colon etc., diminution of liver dullness can only be considered as suggestive if the dullness is lost as far as the mid-axillary line and beyond, posteriorly. Besides, unless gas escapes under pressure, as from a distended stomach, it can hardly get in between the liver and the costal parietes and thus produce this sign.

*Blood pressure, pulse and temperature*—In the 65 cases out of 116 where the blood pressure was recorded on admission, only 7 cases registered a pressure of below 100 mm systolic, of these 7, five were below 80 mm systolic—mostly late cases. The average pressure recorded were 108 mm systolic. This is quite in a keeping with the findings of others. Similarly the pulse and temperature readings showed comparatively identical findings. Fifty-five cases had a pulse rate below 100. Forty-seven cases had a pulse rate of above 100 of which 42 were of more than 12 hours' duration. Two cases registered a pulse of 120 and above within 6 hours of perforation, both were fatal. The large majority of cases, 62, registered a temperature on admission between 97° F and 98° F, 40 cases between 93° F and 100° F and only 14 had a temperature of above 100° F, of these 12 were late cases of duration 12 hours or more.

It is apparent from a study of these figures that actual shock in the early stages of perforation is the exception, and to quote Moynihan here would be apt, "We must therefore not less in the interest of accuracy than in that of the welfare of the patient cease to use the word 'shock' in this connection. Shock, it is true, comes later in these cases. It comes when peritonitis has developed, but peritonitis is not perforation, it is a late and preventable sequel to perforation. It is the perforation we seek to recognise, the peritonitis we seek to forestall." However, it is worthwhile noting that there were 2 cases where death appeared to have been directly caused by collapse within 6 hours of perforation. It is also seen that rise of temperature above 100° F, occurs in late cases and thus, cases which register high temperature within the first 12 hours of onset of pain are unlikely to be acute peptic perforations.

#### DIAGNOSIS

In the large majority of this series, the problem of diagnosis was usually an easy one. But in the slow 'Leaking type' and in other atypical varieties the clinical picture was often misleading. The classical triad, 'free gas, free fluid and absent intestinal sounds' is associated with late cases with diffuse peritonitis and a grave prognosis, and it may be noted that it was present only in less than a third of the cases, most of which were late. Cases must be diagnosed earlier. The association of sudden onset of pain with a positive 'pointing sign' a rigid scaphoid tender abdomen and a full bounding but not fast pulse, should leave no doubt as to the diagnosis in most instances. Some attach a great deal of importance to audible heart sounds over the abdomen, particularly lower down—it is supposed to indicate free gas in the peritoneal cavity. I have on many occasions found this sign positive in cases of intestinal obstruction, ascites and even in normal abdomens, as well as in perforative peritonitis, and as such I feel that no special significance need be ascribed to it.

Other diagnostic measures have been employed and of these, X-ray examination of the abdomen, both fluoroscopic and a plate, is most valuable and reliable, particularly if carried out in the upright position. In fact, this is the only really satisfactory method of demonstrating a pneumo-peritoneum. It is a matter of regret that

we do not employ the test oftener. In 2 cases where I have screened the patients, I have been able to demonstrate free gas under the diaphragm. Naturally, like most other investigations it is not an absolutely fool-proof test. Estes and Bennet quote 72 per cent positive findings in their series of 80 cases. De Bakey in his monumental analysis of nearly 12,000 cases found radiographic evidence positive in 67.4 per cent in a collected series and 64.6 per cent in his own. In order to get a greater frequency of positive plates Ochsner and De Bakey have suggested injection of air through a duodenal tube which is first passed and the stomach contents aspirated, about 30 to 50 c.c. of air is then injected and the plate taken in left lateral decubitus and also in the sitting position. Another measure suggested and practised is, diagnostic aspiration of the peritoneal fluid. I have attempted this twice, though I must confess, that the smears of aspirated fluid when examined microscopically revealed little. In one case there were a few pus cells but no organisms of blood particles. Both were definite cases of duodenal perforations and the aspirations were carried out on the operation table just before the operation. Besides the doubtful value of this procedure there is always the risk of perforating the intestines which may be matted and adherent to the parietes. The aspiration is done with an ordinary lumbar puncture needle after raising a small novocain wheel under the skin and the usual sites chosen are the supra-pubic region in the mid-line 1 inch above the symphysis pubis after emptying the bladder, or the right flank. The exudate in the early stage is thin and can be easily aspirated though the amount is often quite small, but sufficient to make a smear which is stained with Gram's stain and examined for organisms, etc. A small drop is put on another slide and examined under a cover slip for polymorphs, pus cells, food particles, etc. Normally the peritoneal fluid does not contain polymorphs, an excess of which always collects in early peritonitic exudate.

Peritoneoscopy is another procedure which I feel, should prove more valuable than a mere diagnostic aspiration. The procedure is simple, an ordinary cystoscope with an attachment for pumping in air will serve the purpose. It can be done under local anaesthesia. Though in the first few cases interpretation will be difficult, with increasing experience it may be possible to make an exact pre-operative anatomical and pathological diagnosis in many cases. In the present series no case was subjected to a peritoneoscopy. Peritoneoscopy has its disadvantages, the distension of abdomen following inflation of air being the most distressing of all. The method is still in its infancy but it is worthwhile to employ it in doubtful cases, particularly those where the roentgenological evidence is wanting, and short of an exploratory laparotomy diagnosis is in doubt. And, as in most doubtful cases one plays safe and falls back on an exploratory laparotomy, one may find consolation in the words of Lord Moynihan—"To make an accurate anatomical and pathological diagnosis is a delight, but to reach a decision that whatever and wherever the trouble, the sooner measures of rescue are adopted, is a cardinal obligation."

*(To be continued)*

# Report of the Clinical Conferences

AT THE TATA MEMORIAL HOSPITAL, BOMBAY

Conf on 19-44

## HAEMANGIOMA OF THE SKIN

A case of Haemangioma of the skin treated with radon seeds presented by **Dr D R Meher-Homji** A baby of 6 months, with an haemangioma on the skin of left knee It measured  $1\frac{1}{2} \times 1$  cms and was treated by radon seeds Two seeds of 0.7 mcs each were inserted deep to the lesion and within six weeks there was complete disappearance of the haemangioma except at one edge

## CAVERNOUS HAEMANGIOMA OF THE LIP, CHEEK AND TONGUE

A case of cavernous haemangioma of the lip, cheek and tongue presented by **Dr E J Borges** A young lady of 21 with congenital haemangioma of the lower lip, whole of tongue and left cheek As the haemangioma on the lower lip caused an unsightly pouting of that structure, it was decided to treat only the lip with radon seeds The result and considerable improvement was demonstrated One interesting point in this case was that she one day had severe haematemesis for which she was admitted to the K.E.M Hospital The bleeding probably came from an angioma in the oesophagus An oesophagoscopy was not attempted later here because of the risk of fatal bleeding A discussion of the various treatments for cutaneous angioma followed in which the merits of radium, X-rays, sclerosing solutions and CO<sub>2</sub> were discussed

## HODGKIN'S DISEASE

A case of Hodgkin's Disease presented by **Dr E J Borges** (#3690) A 25 year old woman who first came in January, 1943 with a six months' history of lumps in the neck and axilla with occasional fever Biopsy showed Hodgkin's disease associated with tuberculosis X-ray treatment to the nodes made them disappear except in the axilla where the response was tardy and incomplete Returned in June, 1943, with complete regression of nodes in the left neck and axilla and appearance of nodes in right neck and axilla, these were treated and almost completely regressed Returned in January, 1944, with recurrence in the left neck, left axilla and mediastinum Treated again and shown today with regressing nodes Dr Borges commented on the remarkable good health of the woman and the repeated response to radiation, and the absence of an enlarged spleen He asked how often could this radiation be repeated and wanted to know from the pathologists what chances this woman had of developing Hodgkin's sarcoma Dr K P Mody said that this woman had already had as much radiation as one could give her Dr A V Baliga said that the presence of tuberculosis in association with the disease might have been responsible for the incomplete regression in this case Dr V R

**Khanolkar** in replying to a question asked by **Dr Borges** as to what were the chances of the case being changed into a Hodgkin's sarcoma said that no definite answer could be given but judging from the available literature it was unlikely that this case would run the course of a Hodgkin's sarcoma

*Conf on 8 9-44*

#### CANCER OF THE LUNG

A case of cancer of the lung was shown by **Dr E J Borges** (†7755) The patient gave history of cough and pain in the chest and no physical signs except slight impairment of note X-ray examination showed a large shadow with well defined margin in the upper half of the right lung **Dr L H Athle** demonstrated the lateral roentgenograms showing that the mass was situated in the posterior half of the chest Sterioscopic examination showed that the growth extended to the border of the mediastinum and that the hilum was definitely involved There was an area of cavitation at the base due to degeneration In density and configuration this growth was like the peripheral type but its proximity to the hilum would make it a difficult proposition for surgery or radiation He showed the skiagrams of a treated case of peripheral type of lung cancer before and after treatment The growth had almost completely disappeared with the treatment The hilar types do not respond to radiation therapy so well **Dr Borges** enquired as to how one could distinguish an interlobar empyema from a growth of this type, because he had obtained pus-like material on aspiration biopsy **Dr P H Kronenberger** described the biconvex margins in the lateral skiagram characteristic of interlobar effusion **Dr Borges** said that the aspiration biopsy showed evidence of malignant tumour and that surgery should be attempted in this case A thoracotomy done later showed a large growth in the upper part of the lower lobe fixed to the posterior wall and also involving the right hilum

#### CARCINOMA OF STOMACH

**Dr D J Jussawalla** described his findings in a 26 year old male For 5 months, he had suffered from indigestion He had a lump in the abdomen of 4 months' duration He had scars from tuberculous adenitis some years ago A hard globular, movable lump was felt in the epigastrium A provisional diagnosis of carcinoma of stomach was made **Dr Athle** showed the X-ray films which revealed a well marked filling defect in the lower half of the stomach The defect was of intrinsic nature and therefore a malignant disease of the stomach with a large extragastric mass was the obvious diagnosis **Dr Borges** suggested the possibility of a tubercular mass involving the stomach and referred to the man's history and the mobile nature of the mass **Dr Athle**, agreed that tuberculosis of the stomach was known to produce exactly the same type of filling defect as growths but this lesion was exceedingly rare as shown by **Broaders** who got only one such case among the 2,000 stomach operations at the Mayo Clinic He further suggested that the age of the patient and the

nature of the mass were quite consistent with the diagnosis of a lymphosarcoma involving the stomach. On radiological grounds alone it was not possible to give an absolute diagnosis between carcinoma and lymphosarcoma. An exploratory laparotomy was performed and a biopsy from the mass showed lymphosarcoma. A large growth was found enveloping the distal half of the stomach and the lesser omentum. Radiation therapy was instituted following the operation.

#### A CARCINOMA OF THE BASE OF THE TONGUE

**Dr L H Athle** showed a case of carcinoma of the base of the tongue with unilateral neck metastasis († 6173). He had plenty of disease at the end of a full course of X-ray therapy but 4 months later he was completely free from any evidence of disease. This case was a proof of the fact that radiation effects continue for some time after the cessation of the therapy and that regression continues to take place for some weeks. It was important to remember this in considering additional X-ray therapy or supplementing with radon seeds. **Dr Borges** asked if one could prescribe an exact cancericidal dose in these cases. **Dr Athle** replied that this could not be definitely fixed and was a matter of experience and judgment. If the exact dose was known many more cases would be cured.

#### CARCINOMA OF THE TONGUE

A case of carcinoma of the tongue on the dorsum of the anterior third of the tongue near the midline presented by **Dr L H Athle** (†7632). This was a very unusual situation. The lesion consisted merely of a small hard pea-sized nodule by the side of a small fissure. A biopsy confirmed it to be a squamous carcinoma grade II. This man was under X-ray treatment through an intra-oral cone.

*Conf on 15 9-44*

#### GASTRIC ACIDITY IN DISEASE

**Mr S D Ambegaokar** read a paper on "Gastric Acidity in Disease".\* He emphasised the importance of gastric analysis in various diseases of the stomach and referred to a few cases of cancer of the stomach with hyperchlorhydria.

*Discussion*—**Dr R G Modak** said that he was surprised to note hyperacidity in three cases and asked whether cancer in these cases originated from previous ulcer. **Dr E J Borges** quoted an incidence where a consulting physician ruled out a case of stomach cancer because of hyperacidity. The patient returned within a month with typical advanced cancer and died three months later. He concluded that gastric analysis should not be given undue importance. **Dr L H Athle** remarked that this study is a very remarkable contribution because it would help to prove the fact that cancer was not necessarily associated with achlorhydria. Clinical and radiological findings in favour of the diagnosis of cancer should not be discarded, simply because there was hyperchlorhydria. The atrophic gastritis associated with gastric cancer might be responsible for hypo or achlorhydria, while a hypertrophic gastritis may produce hyperacidity as it is seen in some cases. **Dr A V Baliga** remarked that

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\* This paper will appear as an original contribution in a future issue of this journal.



more the gastritis due to the obstruction at the pyloric end, less is the degree of acidity Dr V R Khanolkar concluded that before arriving at a definite conclusion as to the diagnosis of cancer of stomach, one should take into consideration all the available methods of investigations, clinical, radiological and biochemical etc, as none of the methods could be used to the exclusion of others

#### MELANOMA OF THE ALVEOLUS

A case of Melanoma of the Alveolus presented by Dr V V Gharpure (†7519) A Gujarati Hindu male of 57 was referred to the Tata Memorial Hospital for a growth on the right upper alveolus Duration  $1\frac{1}{2}$  years Patient gave a history that he got his right upper teeth removed two years back The wound healed well Six months later he noticed a small ulcer on the right upper alveolus It went on increasing in size for which he consulted a doctor who referred him here On examination of the oral cavity it was noticed that there were pigmented patches on the tongue, cheek, soft and hard palate and throat extending into the larynx There was seen a fungating ulcerated lesion on the right upper alveolus spreading to the hard palate *Laboratory investigations* Urine examination negative, Melanin not found Hb 88 per cent R B Cs 44 millions per cmm, W.B.Cs 7000 per cmm *Differential white cell count* P 69, E 2 M 3 L 26 per cent *Kahn test* Negative Blood, Sugar 976 mgms per cent Biopsy of the alveolus was done and reported as fibrous epulis Another biopsy was done from a pigmented patch on the soft palate and reported as malignant melanoma after studying the case clinically The diagnosis of the biopsy of the alveolus was revised as malignant melanoma *Treatment* An antrotomy was done and an attempt was made to remove the tumour on the alveolus as much as it was possible Naked-eye appearance (D 860) A specimen of excision of an ulcerated growth with a portion of maxillary bone The ulcer had everted edges and measured  $2 \times 3\frac{3}{4}$  cms The edge of the ulcer showed areas of brownish pigment On cut section the brownish pigment was seen in the greyish tumour tissue Histological examination of the tumour showed interwoven spindle shaped cells The cytoplasmic outlines were indistinct The nuclei were spindle and ovoid in shape, 1-2 small nucleoli and fine deeply basophilic chromatin granules Few mitosis seen At places there was a suggestion of palisading of the nuclei such as one sees in neurinomas At one place the tumour was seen in continuity with the surface epithelium Areas of intracellular and extracellular brownish pigment Dopa's reaction showed melanin pigment both intra and extracellular in distribution *Diagnosis* Malignant Melanoma

Dr V V Gharpure said that this was a very interesting case of melanoma of the oral mucous membrane We have studied before two cases of melanoma of the oral cavity One was of the lower lip (†357) and the other was of the hard palate (†60) The age of the lip case was 63 and the palate case was 54 Gotshalk<sup>1</sup> et al have reported a

1 Gotshalk, H.C., Teschner, C.E., & Smith, J.W., Arch Path 3 762 765, 1940

case of melanoma of hard palate in a female aged 28 which metastasised to the lungs. We have also seen melanomas of the mucosa in other regions such as one case of vulva (†6961) and one case of tonsil (†A 245). There was one case of melanoma of the anus in the K. E. M. Hospital museum on which a P. M. was done. Dr A. V. Baliga said that skin melanoma were much more common than melanomas of the mucous membrane. Dr V. R. Khanolkar said that Negroes get very little melanomas. From the histological material he studied from the K.E.M. Hospital he thought that the melanomas usually started at the less pigmented areas of the skin.

#### LIPOSARCOMA OF BONE

A case of Liposarcoma of Bone presented by Dr V. R. Khanolkar (†3208). A Muslim woman 24 years old was seen at this hospital in October, 1943. Her complaint was that she had noticed some pain on the outer aspect of the left thigh four months previously. The pain had subsided since that time but was followed by a feeling of discomfort on walking in the lower part of the back. This discomfort had gradually increased and the patient began to notice some pain in the back when lying on the left side. There was no history of cough, fever or loss of weight. On examination she was found to walk with a slight limp, but did not show any stiffness when getting up after lying down or sitting. There was a tenderness along the left ileum over the crest of the bone. An ill-defined mass was felt on the posterolateral surface of the bone. No restriction of movement of the left hip joint was noticed. An expansile pulsating tumour of the left ileum was seen on screening. The patient was advised to return for a formal biopsy and X-ray studies. She did not return till eighteen months later during which time she had been treated outside. The swelling had grown three times its former size and there was considerable loss of weight. X-rays showed an involvement of the 5th lumbar vertebra and the upper part of the femur, besides destruction of the left ileum and damage to the sacrum. The disease had been diagnosed as osteogenic sarcoma and osteolytic sarcoma on the basis of the X-ray studies outside. A formal biopsy showed the tumour to be made up of large cells arranged loosely or in an alveolar formation. The nuclei were small, hyperchromatic and eccentrically or centrally situated. The cytoplasm contained abundant lipoid material. The tumour was very vascular. On the basis of the histological structure the tumour was diagnosed as a lipogenic sarcoma of the bone. Dr Khanolkar stated that since its first description by Ewing in 1928 and Stewart in 1931 six cases had been described in the available literature. There was however much controversy whether these new growths were primary tumours of the bone or whether the bone was secondarily involved. Ewing had mentioned that the tumours receded after radiation and it was a pity that the woman went away without adequate investigation and treatment in 1942 when the tumour was small and could probably have been controlled by radiation therapy.

# Critical Notes and Abstracts

## TEST FOR HYPERSENSITIVITY TO SULFONAMIDES

Estimates indicate 10 to 15 million persons receive one of the sulfonamides each year. The tendency of the sulfa drugs to produce reactions of hypersensitivity such as fever, dermatitis and conjunctivitis must be borne in mind when use of one of these chemotherapeutic agents is contemplated. Incidence of hypersensitive phenomena following use of sulfa drugs varies from 2 to 36 per cent. Sulfanilamide, sulfapyridine, and sulfadiazine induce sensitization with about the same frequency, sulfathiazole is more likely to produce sensitization than the others.

W B Leftwich, (Bull Johns Hopkins Hosp 74 26, 1944) presents findings suggesting that an intradermal test, using blood serum from patients receiving sulfonamides, may be useful in diagnosis of sulfonamides hypersensitivity before therapy is started. A specific serum must be used for each sulfonamide. The material used for the skin test consists of serum obtained from patients receiving a sulfonamide therapeutically in dosage sufficient to maintain blood levels of 2 to 25 mg per cent. The test is simple to perform, may be easily and quickly interpreted, and was found to be reliable in diagnosis of drug sensitivity in 28 out of 30 cases.

It is hoped that this test may be useful, both in the differential diagnosis of drug reactions, and perhaps as a precautionary measure before starting sulfonamide therapy in patients who have previously received one of these compounds. The fact that positive skin tests may be so consistently obtained in hypersensitive persons is additional evidence that drug sensitivity is an allergic reaction. Leftwich says, the sensitizing antigen may be a sulfonamide-plasma protein combination which occurs in vivo in the circulating blood of patients during sulfonamide therapy, the sulfonamide perhaps acting as a haptene.

Since the test is specific for each sulfonamide, the patient should receive an intracutaneous test with serum containing the sulfonamide with which he is to be treated. Serum for use in testing may be obtained from patients who are being treated with one of the sulfonamides, whose blood cultures are negative, and in whom the serologic test for syphilis is negative. Twenty to 30 cubic centimeters of blood is allowed to clot in a sterile centrifuge tube.

The clot is separated from the container with a sterile glass rod, and the tube centrifuged at high speed for twenty minutes. The serum is then pipetted off, placed in sterile, rubber-stopped containers, and checked for sterility. Serum may be kept at refrigerator temperature, it has been preserved in the frozen state for as long as two months with no effect on its ability to evoke positive skin tests in sulfonamide sensitive patients.

The test requires use of tuberculin syringes and 26-gage needles. Into the flexor surface of the forearm, 0.05 cc of the sulfonamide containing serum, and 0.05 cc of control serum are injected intracutaneously at separate sites. Sizes of the wheal and erythema produced are measured immediately after injection and at intervals of five minutes for twenty minutes. The initial wheal size is 6 or 7 mm in diameter, and in negative tests and in the controls the size of the wheals increases only 1 or 2 mm (up to 7 or 8 mm in diameter) and an area of pale redness covers a small area up to 20 mm in diameter.

Positive tests showing definite hypersensitivity reveal an immediate increase in the size of the wheal produced by the sulfonamide containing serum up to 12 to 18 mm in diameter with intense erythema 30 to 40 mm in diameter, and the development of pseudopods when the reaction is marked.

A positive reaction becomes maximal in fifteen minutes after the injection, and fades in thirty minutes, so that by the end of an hour and a half all traces of the wheal are gone. Leftwich says a difference in size in the control wheal and the size of the test wheal of at least 4 mm diameter may be used as a criterion for positivity, rather than absolute size of the test wheal.

#### **GLUTAMIC ACID IN PETIT MAL EPILEPSY.**

Clinical studies by H. Waelsch and J. C. Price (*Arch Neurol and Psychiat* 51:393, 1944) indicate that the effectiveness of dl-glutamic acid (an amino acid) in reducing attacks of petit mal in epileptics largely resides in its 1 (+) glutamic acid component.

Administration of dl-glutamic acid hydrochloride to epileptics resistant to usual anticonvulsant therapy resulted in decreased incidence of seizures and increased mental and physical alertness. In about 20 patients suffering recurrent attacks of petit mal unresponsive to other therapy, glutamic acid reduced both frequency and severity of seizures.

Attacks, in a twelve year old boy, were reduced in frequency from 25 to 50 daily to about 5 to 25 by administration of dl-glutamic acid hydrochloride, 12 Gm daily. No more than 8 to 12 Gm of natural glutamic acid was necessary to further reduce the number of attacks. In this patient, personality improved when either the racemic or natural form of glutamic acid was given.

Reduction in frequency of attacks roughly proportional to take dose (14 to 28 Gm) of 1 (+) glutamic acid was observed in a twenty three year old man in whom other forms of antiepileptic therapy had been ineffective or poorly tolerated.

The authors indicate that glutamic acid is effective only in treatment of petit mal epilepsy, it is ineffective in grand mal and may even increase the number of seizures.

# Reflections & aphorisms

## PHYSICIAN, PATIENT AND PHYSICK

Of those diverse gifts which God bestowed on man, this of Physick is not the least but most necessary, and especially conducing to the good of mankind. Next therefore to God in all our extremities, we must seek to, and rely upon the Physician, who is the Hand of God, and to whom He hath given knowledge. It is not therefore to be doubted that, if we seek a Physician as we ought, we may be eased of our infirmities, such a one I mean as is sufficient, and worthily so called, for there be many Mountebanks, Quacksalvers, Empiricks, in every street almost, and in every village, that take upon them this name, make this noble and profitable Art to be evil spoken of, and contemned, by reason of these base and illiterate Artificers but such a Physician I speak of as is approved, learned, skilful and honest. Only this much I would require honesty in every Physician, that he be not over-careless, or covetous, to make a prey of his patient as an hungry Chirurgeon often produces and wire-draws his cure, so long as there is any hope of pay—The leech never leaves the skin until filled with blood. Many of them, to get a fee, will give Physick to every one that comes, when there is no cause, and they do so stir up a silent disease, as it often falleth out, which by good counsel, good advice alone, might have been happily composed, or otherwise cured. A wise Physician will not give Physick but upon necessity, and first try medicinal diet, before he proceed to medical cure. Though the patient be averse, desire help and refuse it again, though he neglect his own health, it behoves a good Physician not to leave him helpless. But most part they offend in that other extreme, they prescribe too much Physick, and tire out their bodies with continual potions, to no purpose. Aetius will have them by all means therefore to give some respite to nature, to leave off now and then, after a deal of Physick to no purpose, left to themselves, many have recovered. Many things are necessarily to be observed and continued on the patient's behalf. First that he be not too niggardly miserable of his purse, or think it too much he bestows upon himself, and to save charges endanger his health. Another thing is, that he do not out of bashfulness conceal his grief, if ought trouble his mind, let him freely disclose it. He must be willing to be cured, and earnestly desire it. 'Tis a part of his cure to wish his own health, and not to defer it too long. And often out of prejudice, a loathing, and distaste of Physick, he had rather die or do worse, than take any of it. Barbarous immanity and folly to be deplored, so to condemn the precepts of health, good remedies, and voluntarily to pull death, and many maladies, upon their own heads.

ROBERT BURTON

# The Indian Physician

VOL IV NO 2

FEBRUARY 1945

WHOLE NO 38

## Original Contributions

### PERFORATED PEPTIC ULCER OF THE STOMACH & DUODENUM

BASED ON A STUDY ON 116 CASES

By

P K SEN, M S (Bom)

K E M Hospital, Bombay

(Continued from page 14)

#### TREATMENT

**Operation**—One hundred and six cases, 84 duodenal and 22 gastric were operated in this series of 116 cases. Of these 106, 43 died, a total operative mortality of 40.5 per cent. The operations include those late cases where only drainage of the peritoneal cavity was carried out. The procedures adopted were as follows—

	Duodenal	Gastric	Total
1 Simple closure of perforation	28	9	36
2 Simple closure + Omentopexy	54	0	54
3 Closure + Gastro jejunostomy	1	1 (Pyloric)	2
4 Drainage only	1	4	5
		Total	100

The incisions employed were as under :—

Upper right para median  
Mid line  
Right trans-rectus

	100
	5
	1
Total	106

The upper right para-median incision is to be preferred in most instances even though the mid-line offers a quicker approach, the incidence of sepsis and burst abdomen is high in this series, about 40 per cent as compared to 18 per cent in the right para-median.

In closing the perforation the usual technique was followed in most. The perforation was sutured by means of a through and through 00 chromic intestinal catgut and when inverted by means of a sero-muscular purse string or succeeding tiers of Lembert sutures placed transverse to the long axis of the gut to prevent narrowing. In 63 cases the omentum or other peritoneal folds were used to reinforce the suture line. I have lately in some cases used instead of the omentum, the round and falciform ligaments of the liver as recommended by Finney of Baltimore, Md, and found it very serviceable. The round ligament and the anterior margin of the falciform ligament is detached from the anterior parietal peritoneum and left at-

tached to the porta hepatis. This fold is then wrapped round the first part of the duodenum and anchored with a few interrupted cat-gut sutures to the sero-muscularis. This peritoneal fold has more substance and is almost fibrous in consistency and constitutes a much stronger and safer barrier than the tenuous fold of omentum which is usually and almost apologetically selected in most cases. Also, in large perforations with fixable edges this method is very satisfactory. The terminal part of the fold is rolled up into a small plug which is wedged into the perforation and sutures applied all round through the healthy sero-muscularis and the mobilised peritoneal ligament. There were 17 deaths out of 36 cases where only simple closure was done, a percentage mortality of 47.2 per cent and in those where additional reinforcement was used 20 died out of 63, a mortality of 31.7 per cent.

Closure and gastro-jejunostomy was done only in 2 cases. One was a sub-acute duodenal perforation with considerable fibrosis, the other, a pyloric ulcer. One, the pyloric ulcer case died, a mortality of 50 per cent. Simple drainage was merely done in those very late cases (mortality 100 per cent) where the patient's condition did not permit of any prolongation of the operation. Drainage of the peritoneum was instituted in the large majority of the others where there was plenty of exudate, usually both a supra-public drain in the pouch of Douglas and another in the right flank draining the Morrison's pouch. During operation one must be very careful in removing by mop and suction all collection from this important peritoneal cul-de-sac, as the incidence of post-operative subphrenic abscess is by no means very small as later figures will show. The wound itself was drained only in 10 cases. Occasionally, particularly in duodenal perforations, the opening is so tiny that a small flake of lymph of fibrinous pus may cover it and thus it may be missed. Baker (1920) and later Nisbet and Morrow recommended the oral administration of 2 to 3 ozs of a solution of methylene blue prior to operation to facilitate the search for a perforation. If this method is routinely followed, I am sure a great deal of time will be saved and not only small, but the rarer, multiple perforations will never be missed.

An accessory therapeutic measure at operation that has been tried in a few cases by one of our colleagues is the production of an artificial haemoperitoneum before closing up the laparotomy wound. After suture of the perforation one or two of the larger omental vessels are divided and about 100 to 150 ccs of blood allowed to collect in the peritoneal cavity. The number of cases in which this measure was tried are only a few and therefore it is difficult to evaluate the exact position of this procedure. But considering that local auto-haemotherapy for other inflammatory conditions, i.e., for diabetic carbuncles etc., has not been found of any great help, it is doubtful if this procedure will have a definite effect on the final end results. However, the method is worth a wider trial.

*Local Sulphanilamide*—Sulphanilamide powder may be dusted over the suture line and freely in the peritoneal cavity or poured in

as a solution This was done in only 16 cases Of these 16, eight died—a mortality of 50 per cent, also of these 16 cases, 3 developed localised peritoneal abscesses while in the remaining 90 cases where local sulphanilamide was not used only 5 developed such a complication The place of local sulphanilamide therapy in suppurative peritonitis is not secure, nor is it based on rational pharmacological grounds We know that sulphanilamide and the sulpha drugs in general are quickly rendered ineffective in the presence of pus, and as such, the salutary effect of local sulphanilamide in perforated peritonitis is at best an evanescent one

Other and more radical measures like excision of ulcer and pyloroplasty and partial gastrectomy have been adopted and practised in preference to simple closure by many Continental and American surgeons, notably Finsterer and Gerhardt in Vienna, Judine in Russia and Graham in America In England also these methods have found favour with some surgeons notably Gilmour and Saint who quote a mortality of 27 per cent in partial gastrectomies practised for acute peptic perforations The figures of Finsterer are astoundingly low, about 2 per cent in a large series of partial gastrectomies done for acute perforations of both stomach and duodenum Excision of ulcer and pyloroplasty has been practised by some American surgeons for perforated duodenal ulcers only, notably Finney In general, the majority of American and English surgeons favour the conservative method of local closure, while the Continental surgeons are warm advocates of more radical procedures Judine found the mortality incidence following simple closure was 42·7 per cent and that following partial gastrectomy only 8·9 per cent In none of the cases in the present series of this hospital has any radical measure been adopted and I hold this to be quite correct, as the first consideration of the surgeon is the treatment of perforation and prevention or spread of peritonitis and not the treatment of the ulcer itself, and therefore only the minimum of operative procedure compatible with the safety of a patient who is already desperately ill, should be practised, gastroenterostomies should be reserved for only those cases where, after suture of perforation the lumen of the gut becomes unduly narrow One cannot, however, entirely overlook the brilliant results of partial gastrectomies done by Continental workers—but it seems possible that without proper choice of cases i.e., to use such a procedure in a consecutive series irrespective of duration and risk may not produce such encouraging results Conversion of the perforation into an artificial fistula by doing a gastrostomy or duodenostomy through the perforation is advised in large openings with friable edges, but is only practicable in gastric ulcers High perforations of the stomach near the cardia may thus be tided over and the fistula closed at a later date for large duodenal perforations it is better to occlude the duodenum completely and perform a gastroenterostomy.

*Anaesthesia*—Of 160 cases operated upon the anaesthetics were as follows—



1	Spinal (Stovaine, Barker's—also 10 cases of Percaine 1-1500)	56 Cases
2	Spinal + Intravenous Sodium Pentothal	7 "
3	Spinal + General	12 "
4	General (mainly ether or mixture)	17 "
5	Peri-dural + Intravenous	2 "
6	Local	9 "
7	Local + General	3 "
Total		106 cases.

Spinal anaesthesia has been used in the majority of cases and is the most satisfactory 15 to 2 ccs of stovaine (Barker's solution) produces anaesthesia upto nearly an hour and affords good relaxation. The combination of spinal and intravenous anaesthetics is as completely satisfying as the combination of spinal and general (ether or mixture) is aggravatingly irritating. The injection of morphia 1/8 to 1/6 grain intravenously in the later phases of a prolonged operation under spinal has been found very satisfactory, both as regards prolongation of anaesthetic effects and the subsequent sedation of the patient. General anaesthesia should be reserved only for cases with low blood pressure, where local and intravenous should still be preferred. Apart from the danger of aspiration broncho-pneumonia and insufficient relaxation of muscles which may be obliterated by an intra-tracheal tube, inhalation ether or chloroform anaesthesia is often attended by tumultuous diaphragmatic respiratory excursions which make manipulations extremely difficult. The introduction of cyclopropane, however, does away with all these disadvantages and it can be used in the worst cases. It is still not readily available in plenty and therefore cannot be used as a routine. Local anaesthesia, with proper technique is quite satisfactory with or without intravenous pentothal sodium or morphia. It is, however, somewhat time consuming. In late cases it has a decided advantage.

The mortality attendant on the various types of anaesthetics has not been worked out as the conclusions would be erroneous for there are a large number of late cases in this series, and thus a comparative index will not be accurate.

*Post-operative Management—Fluids*—The post-operative management of such cases is of paramount importance and plays a major part in their ultimate recovery. From the cases studied in this series it is at once apparent that a planned regime of treatment was not followed in the majority as a general routine. Fluids were administered intravenously in 71 out of 106 cases operated upon, and in 62 of these, the average amount was only about a pint a day, administered fitfully. In 20 cases only rectal saline was given, and in 15 cases no fluids whatever were administered except small sips of water. Thus it is obvious that one of the main causes of the high operative mortality in this series is the failure to supply adequate quantities of fluid. Here I should like to put in a plea for the administration of fluids (saline, glucose saline, plasma) by continuous venoclysis in all such cases controlled by water balance charts, haematocrit readings, and clinical signs in the lungs. The amount of fluid administered in most of the cases of this series has been woefully inadequate. Barely a third of the daily 2,000 to 3,000 c.c of fluid which are required in such

cases have been supplied. The bogey of pulmonary oedema in massive fluid administration, I feel, has been grossly overrated. In this series only 2 patients died of pulmonary oedema, both very late cases. With properly controlled fluid therapy the dangers of overloading circulation or of pulmonary oedema is very slight or nil. Whole-blood transfusions are not usually needed excepting in late septic complications. Only 5 cases in this series received blood transfusions, all for late sepsis.

**Sulphonamides**—Sulpha drugs have been used, mostly by intramuscular injection of soluble sulphonamides (prontosil, soluseptasine) and in few cases by oral administration of sulphapyridine (M & B 693). Thirty-two operated cases have been thus treated mainly from 1938 onwards. Of these, 13 died, a mortality of 40.6 per cent. In the rest, 74 cases (before 1938) sulpha drugs were not used and there were 31 deaths, a mortality of 41.8 per cent, with hardly any difference from those treated with sulpha drugs. These figures, however, should not be taken at their face value, as in most cases the sulphonamide therapy was insufficient in dosage, spasmodic in administration, and bereft of any definite control whatsoever.

**Gastric suction**—One of the greatest contributions of recent years to the treatment of peritonitis and ileus is the continuous Wainman drainage of the stomach and duodenum by means of an indwelling duodenal tube. The tube was used in 30 cases, but only in 7 cases was it used as a continuous measure. When we consider that the largest number of deaths in this series was due to ileus from general peritonitis, the importance of this form of therapy leaves no room for doubt. This type of continuous gastro-duodenal aspiration should be a routine in all cases. For the prevention and treatment of ileus many other remedies, e.g. pitressin, acetyl choline, hypertonic saline, were used but found to be mostly ineffective. I have used small doses of morphia gr 1/6th every 6 hours as a routine and found it more useful than any other drug in the prevention and treatment of ileus.

#### COMPLICATIONS

The incidence of various complications following operation in this series is summarised below (Total number of operations, 106). Their respective mortalities are also considered.

Nature of complication		No of cases	Percent incidence	No of deaths	Mort Percentage
1	Post-operative collapse and shock	20	18.8 p.c	12	60 p.c
2	General Peritonitis + Paralytic Ileus	21	19.8 "	12	57 "
3	Peritoneal Abscesses:—	8	7.5 "	6	75 "
	(a) Sub-phrenic	5	4.7 "	3	60 "
	(b) Perigastric	1	0.9 "	1	100 "
	(c) Pelvic	2	1.8 "	2	100 "
4	Plastic Ileus	1	0.9 "	1	100 "
5	Fistula	3	2.8 "	3	100 "
6	Pyloric Stenosis (One discharged against medical advice and Gastroenterostomy done on the 21st day in the other)	2	1.8 "	Nil	Nil
7	Wound Infection (12 Major, 6 slight)	18	16.9 "	Nil	Nil
8	Burst Abdomen	3	2.8 "	1	33 "
9	Pulmonary Complications	38	35.8 "	11	28.9 "
	(a) Bronchitis and Basal Congestion	6	5.0 "	Nil	Nil
	(b) Lobar Pneumonia (15 rt. base, 1 lt. base, 2 bilateral)	17	16 "	8	47.6 "

Nature of Complication	No of cases	Percent Incidence	No of deaths	Mort. Percentage
(c) Broncho-Pneumonia	5	4.7 "	4	80 "
(d) ? Massive Collapse (Only 1 proved radiologically, rest doubtful)	5	4.7 "	Nil	Nil
(e) Lung Abscess	3	2.8 "	1	33 "
(f) Acute Pulmonary Oedema	2	1.8 "	2	100 "
10 Pulmonary Embolism ?	1	0.9 "	1	100 "

The large number of cases which developed and died of post-operative collapse and shock is partly due to the greater number of late cases in this series and partly to the insufficient pre and post-operative fluid therapy. General peritonitis and its attendant paralytic ileus was next responsible for a high mortality, yet it is worth noting that only 21 cases out of 106 operations developed general peritonitis with a mortality of only 57.1 per cent. Localised peritoneal abscesses developed in 8 cases (7.5 per cent), 5 subphrenic, 1 perigastric and 2 pelvic. The incidence of subphrenic abscess is low (4.7 per cent) as compared with De Bakey's 7.2 per cent. Even then this is a complication which should be always borne in mind in every case which develops signs of right basal congestion or consolidation with persistent and irregular elevation of temperature and a leucocytosis of 20,000, or over, specially if the response to treatment of pneumonia is poor. In this connection the value of fluoroscopy as a routine in all persistent basal lesions cannot be too strongly emphasised. Of the 5 cases of subphrenic abscess 2 were diagnosed post-mortem. One was diagnosed by X-ray examination the day prior to death, after which it was confirmed at autopsy. Two were operated upon and drained. One by resecting the 8th rib in the right mid-axillary line (trans-peritoneal approach), the other, a recent case of Mr M. M. Pandya by resection of the last rib on the right side (extra peritoneal approach). Both cases survived. Two cases of pelvic abscess developed and both died without being operated upon, the general condition of the patients being very low. The solitary case of perigastric abscess was not strictly a post-operative complication but actually found during an operation for perforated duodenal ulcer. The abscess was drained and the perforation sutured, but the case died. Plastic ileus developed in only one case, 18 days after operation. Conservative treatment was employed but the patient died within a few days. Fistulae developed in 3 cases (2.8 per cent), 2 duodenal and 1 gastric. The gastric fistula developed in a case of perforated doubtful ulcer cancer. The time of onset in the 3 cases was the 3rd, 8th and 5th days respectively. Conservative treatment was employed in all cases such as gastric suction, albuminous dressings, etc. All the 3 cases died. Pyloric stenosis during the post-operative period was detected in 2 cases, one on the 21st and the other on 25th post-operative day by a barium meal. Gastro-enterostomy was done in one. The other refused operation.

In 18 cases wound infection developed (16.9 per cent), of these 6 were slight but 12 were cases of major sepsis, requiring secondary closure of the wound. In 3 cases the wound gave away, producing a burst abdomen (2.8 per cent). One of these was a case of duodenal fistula with extensive digestion of the wound. The other two were

sutured and one of them died. In De Bakey's series this group (wound infections and burst abdomen) occupied a large place, the incidence is as high as 25.4 per cent. In this series, of the 21 cases of wound sepsis and burst abdomen, 2 were mid-line incisions and the rest para-median, an incidence of 40 per cent and 18 per cent respectively.

By far, the largest and probably the most important group is that of pulmonary complications. Their incidence is very close to De Bakey's figures, who quotes it as 32.8 per cent. In the present series the incidence was 35.8 per cent. The different types of lung affections are tabulated and it will be seen that lobar pneumonia is the commonest, particularly in the right base. Of the 17 cases of lobar pneumonia, 15 were in the right base, 1 in the left and 2 bilateral, and of these, 3 cases died. Five were clinically labelled broncho-pneumonias, 2 of which were confirmed at autopsy as cases of aspiration broncho-pneumonia with acid digestion of pulmonary tissues. The time of onset of pneumonia was on the 3rd, 4th or the 5th pre-operative day. Three cases went on to pulmonary suppuration and abscess formation. One was treated medically, a second by a two stage pneumotomy and drainage after rib resection, and the third was detected only at autopsy. Both the cases treated lived. In 5 cases the clinical picture suggested a massive lobar collapse but was only confirmed in one by a skiagram. The 2 cases of acute pulmonary oedema (both fatal) occurred in late perforated gastric ulcers and within 48 hours of operation. The incidence of pulmonary complications in different anaesthesia employed was about the same, with a somewhat greater frequency in cases where general anaesthesia was employed. The solitary instance of suspected pulmonary embolism occurred in a case of perforated duodenal ulcer where the wound broke down with severe sepsis and a burst abdomen followed which was repaired. On the 10th day following the second operation just as the patient was improving, he suddenly collapsed and died.

*Comment*—The majority of post-operative complications are either preventable or curable by early treatment and so the duty of the surgeon should be to maintain a vigorous and rational post-operative regime and to be constantly on guard in order to detect the onset of any complication. The role of continuous post-operative venoclysis and gastric aspiration has already been stressed. Continuous administration of oxygen through either a nasal catheter or better still, a B.L.B. mask or in a tent is a very necessary step and should be made a routine in all severe cases. Judicious and controlled sulphonamide therapy will prevent or alleviate many complications like pneumonia and the once dreaded spreading peritonitis. In short, since most of the post-operative deaths are due to their complications, they must be detected in time and treated early and vigorously.

#### RESULT AND MORTALITY

The total gross mortality of all the cases of this series, operated or not, is 45 per cent. Of 116 cases, 53 died. Of the 93 duodenal ulcers 37 died and of 23 gastric, 16 died, a mortality of 39.7 per cent and 65.2 per cent respectively. The total mortality figures unfavour-

ably with most American and English figures De Bakey quotes 25.2 per cent as the total death incidence in a series of 16,752 collected cases Stanley Raw in a recent article in the Lancet reports a gross mortality of 14.4 per cent only The figures of S Mohan Rau of Madras approximate our own very closely, in a series of 107 cases the mortality rate was 44.9 per cent.

*Mortality with relation to age*—The maximum age-incidence of perforated gastro-duodenal ulcer in this series has been in the 3rd decade The largest actual number of deaths is in the same age group; of 52 cases, 18 died But the mortality percentage in this group is the lowest The other age-incidences of mortality are tabled below —

	Age in years :						
	9-10	11-20	21-30	31-40	41-50	51-60	61-70
No of cases		6	52	43	18	4	3
No of deaths		5	18	15	11	2	2
Percent Mortality		88.8 p.c	34.6 p.c	45.4 p.c	51.1 p.c	50 p.c	66.6 p.c

It should be noted that the mortality is high both in the very young and the old In De Bakey's series the mortality rate rises with the age-incidence

*Mortality in the sexes.*—There were 111 males with 49 deaths and 5 females of whom 4 died, a mortality of 45 per cent in the male and 80 per cent in the female The high death rate in spite of the low incidence in the female is attributable to the fact that 3 of the 4 female deaths were cases of perforated gastric ulcers which have been already shown to have a much higher mortality than perforated duodenal ulcers De Bakey also quotes a much higher mortality rate in women though he admits the lack of a satisfactory explanation

*Mortality and the situation of ulcer*—The site of perforation bears a direct relation with the mortality, as has been shown repeatedly Below are tabulated the mortality rates of the different perforation sites

Situation	No of cases	No of deaths	Mortality Percentage
Pyloric	5	3	60 p.c
Pre pyloric	2	1	50 "
Lesser curve :			
(a) Near cardia	5	5	100 "
(b) Lower down	9	5	55.5 "
Greater curve	1	1	100 "
Post wall	1	1	100 "
1st Part :			
(a) Anterior	86	33	38.3 "
(b) Posterior	3	2	66.6 "
2nd Part			
(a) Anterior	2		0 "
(b) Posterior			
Unknown	2	2	0 "
Total	116	53	

- Note :—(1) The 100 per cent mortality rate of high gastric perforations on the lesser curve near the cardia  
 (2) That the pyloric and pre-pyloric ulcers have the lowest mortality in the gastric perforations  
 (3) The high incidence of death in posterior duodenal perforations

*Mortality according to duration of perforation*—Perhaps the most cogent single factor in the determination of prognosis in a given case is the time that elapses between perforation and operation An attempt is made here to correlate them with this factor in the accompanying diagram It will be seen that the mortality rate, both for

duodenal plus gastric perforation and separately mounts steadily with the increase in the time interval. Two points are worth noting—one, the low mortality (9.5 per cent) of perforated duodenal ulcers operated within the six hours of perforation and the very high mortality of gastric perforation in the same group. And in the second, that no gastric perforation of 24 hours' duration or more, survived, while duodenal perforations lived when operated upto 48 hours after onset of symptoms. The importance of these two features in estimating prognosis is obvious.

**Mortality and operation**—Total operative mortality in the 106 operations performed was 40.5 per cent. The difference from the gross overall mortality of 45 per cent in the whole series of 116 cases is comparatively slight. De Bakey's figures show an even slighter difference between operative mortality and total gross mortality (25.2 per cent total mortality and 23.4 per cent operative mortality). The high figure of post-operative mortality in this series is mainly due to the inclusion in the list of operations those late cases where only peritoneal drainage was done.

The incidence of mortality in the different operative procedures were as follows—

Procedure	No of cases	No of deaths	Mortality Percentage
Simple closure	86	17	47.2 p c
Simple closure + Omentoplexy	63	20	31.7 "
Closure + Castro Jejunostomy	2	1	50 "
Drainage only	5	5	100 "
<b>Total</b>	<b>106</b>	<b>43</b>	<b>40.5 p c</b>

**Operative Mortality in perforated gastric ulcers —**

22 Cases operated.

15 Died

68.3 per cent. Mortality percentage

**Operative Mortality in perforated duodenal ulcers —**

84 Cases operated

28 Died

33.3 per cent. Mortality percentage

The decidedly lower mortality rate in the cases where omental reinforcement was done as compared with simple closure only is very suggestive and indicates that this step in the operation is not only desirable but necessary.

**Cause of Death**—As far as has been possible an attempt has been made to determine the exact cause of death in each case. This was available in only 53 cases. Autopsy was performed in only 14 cases of this series and as such corroborative evidence of clinical diagnosis was lacking in the large majority. The results are tabulated below.

Cause of death	No of cases	Percentage Incidence
1 Peritonitis (+ Paralytic ileus)	17	14.7 per cent.
2 Shock and Collapse (Post-operative)	14	12.9 "
3 Pneumonias (including Broncho pneumonias)	7	6 "
4 Lung Abscess	1	0.8 "
5 Acute Pulmonary Oedema	2	1.7 "
6 Subphrenic abscess	3	2.5 "
7 Pelvic abscess	2	1.7 "
8 Fistula	3	2.5 "
9 Pulmonary embolism	1	0.8 "
10 Plastic ileus	1	0.8 "
11 Toxaemia (without ileus or pneumonia)	1	0.8 "
12. Burst abdomen	1	0.8 "
<b>Total</b>	<b>53</b>	<b>45 per cent</b>

**END-RESULTS**

Owing to the difficulties in tracing the further histories of these patients satisfactory information was available in very few of these cases. Therefore they have not been dealt with in this paper.

**Reperforation**—Two cases of reperforation were, however, found in this series, an incidence of 1.7 per cent. One was a case of perforated duodenal ulcer which was sutured and reperforated at the same site a year later. The other was also a case of anterior duodenal perforation which was readmitted a year later with signs of reperforation but this time it was a pyloric (probably a "kissing") ulcer which had perforated. Both these cases survived the suture of the second perforation and in a subsequent test meal both showed a very high free HCl curve. Partial gastrectomy was advised in both cases, but refused. The occurrence of reperforation from the old site of perforation and that from a different ulcer must be distinguished, but both groups are of interest in regard to the clinical impression that acute perforation cures an ulcer. Possibly the treatment, cauterization or excision of an ulcer, is based on this hypothesis. The incidence of cure is listed variously by different authors, Grey Turner mentions that only 50 per cent of cases are cured by perforation. The total incidence of reperforation varies with different workers, ranging from 0.69 (Pearse) to 12.1 per cent. Estes and Bennett. The mortality in such cases is lower than others as the patient, made wiser by his previous experience, sees a doctor earlier, and possibly also because of the local peritoneal reaction.

In conclusion, I have to thank all the surgeons, past and present, of this hospital for their courtesy in allowing me to include their cases in this collected series, and the Dean, K.E.M. Hospital, for the use of the hospital records. I must also thank Dr. Hannamshet, my House Surgeon, for collecting the case papers, Dr. Monteiro for the details of autopsy records and all of you for the patient hearing you have given me.

**SUMMARY AND CONCLUSIONS**

1. A consecutive series of 116 established cases of perforated gastro-duodenal ulcers treated during the last 10 years at the K.E.M. Hospital, Bombay, are analysed. Of these 93 were duodenal and 23 gastric. There were no jejunal or gastro-jejunal ulcers. The gross overall mortality was 45 per cent.

2. A definitely earlier age-incidence was found as compared to Western figures. There were only 5 females in this series: 1 duodenal and 4 gastric. The higher incidence of female in gastric perforations is stressed. A seasonal rise of perforations in winter is noted. A low incidence amongst brain workers is found and is keeping with the findings of other workers. A fairly high incidence (6 per cent) amongst professional bus or motor drivers is noted.

3. Certain etiological factors in the immediate production of perforation are described. Amongst other factors the part played by trauma is discussed. Ingestion of food was the most important factor in many.

4 The clinical syndrome as was observed at the time of admission is summarised. Low blood pressure and shock are rarely present. A clinical sign of some value in diagnosis—"The pointing test in peptic perforation" is described. The value of radiography in diagnosis is stressed. The problem of clinical diagnosis and other aids to it are discussed.

5 Operation was performed in 106 of the 116 cases in this series. The total operative mortality was 40.5 per cent. The merits of different operative procedures are discussed. The value of sulphonamides locally is also considered. Spinal with or without intravenous anaesthesia was the anaesthetic of choice.

6 The post-operative treatment of these cases is discussed and a plea made for continuous and controlled venoclysis, Wangensteen drainage of the stomach and oxygen administration, as a routine.

7 The complications and the various mortality factors have been considered in detail. The preventability of most complications is stressed. The incidence of complications, such as, pulmonary complications, subphrenic abscess etc., have been fully discussed.

8 Two cases of reperforation (incidence 1.7 per cent) are reported.

## DISCUSSION

Dr T O Shah said that the steep rise in the number of perforations in the last two years was in his opinion not due to the increase in population in Bombay, because no larger numbers of gastric ulcer cases were seen nor was there a proportionate rise in the number of admissions. He observed that the inferior quality of the food might have been responsible and suggested that investigations in this respect be carried out. He stressed the importance of early signs like boardlike rigidity, obliteration of liver dullness and collection of fluid in the flanks. He further added that in the evaluation of the gravity of these cases, the presence of shock, the condition of the pulse, the blood pressure and the absence of intestinal movements were important. He advocated the use of the greater omentum for the reinforcement of the suture line in preference to the falciform ligament which he thought, might produce a free peritoneal band, later giving rise to a strangulation. He preferred to drain the peritoneal cavity whenever in doubt. He pointed out that a large number of deaths were due to peritonitis and residual abscesses and was of opinion that more frequent drainage would prevent or check these septic complications.

Dr S B Gadgil stressed the importance of skiagraphy in the diagnosis of perforations. He compared the mortality figures of Judin in Moscow (who practised partial gastrectomies for perforated ulcers) of 12 per cent. of Saint in Newcastle of 4 per cent., with the high mortality figures in the present series where only suture of the perforation was carried out in most cases.

Dr A V Balligal said that his impression was that the mortality of operations was lower than mentioned by the speaker. It was probably based on his experience in private practice where patients sought surgical aid earlier. He observed that the higher incidence of perforations was due to higher number of admissions of unperforated peptic ulcers. He also mentioned a case where he had used the falciform ligament for reinforcing the suture after detachment from the abdominal wall. He was of the opinion that there was no risk of it forming a band.

Dr K G Munsiff observed that peptic ulcers were uncommon in Gujaratis as seen from the records of the Sir Harkisondas Hospital where only three cases were treated in the last fifteen years all being males between 20 to 80 years. He mentioned that the majority of patients complained of acute pain in the epigastric region just below the xiphisternum. The use of sulphonamide powder was not favoured by him as in the experience of Army Surgeons it formed into foreign bodies which had to be removed subsequently. He further added that where there was marked distension of the intestine and it was difficult to suture the peritoneum, he found Spencer's W shaped suture of value because it took less time and there had not been in his experience a single case of burst abdomen.

Dr G M Phadke said that in two cases of ruptured colon with faecal contamination of the peritoneal cavity with subsequent recovery the good results obtained were in his opinion probably due to the presence of free blood in the cavity resulting from the incidental injury to the mesenteric vessels. This led him to the use of blood in five cases of acute duodenal perforations with success. He made a plea for further trials of this method.

Dr A E. DeSa stressed the value of radiography in the diagnosis of peptic perforation and showed a radiogram where the presence of gas between the right dome of the diaphragm and the liver, clinched the diagnosis in a doubtful case.

He disagreed with one of the speakers about the value of yearly surveys in conditions like peptic perforation. In this particular 10 year analysis (1934 to 1944) the logical division would be into the first quinquennial period (1934-1939) when the sulphonamides had not assumed the prominence they have now and the second quinquennium, during which the sulphonamides had been freely employed both locally and parenterally.

He also stressed the extreme difficulty of distinguishing coronary thrombosis in the elderly male from a peptic perforation, and made a plea for the more frequent calling in of a physician in a doubtful case.

Dr R G Glinde briefly described some atypical cases which he had treated and also said that



the case of large perforation of the posterior wall of the stomach was in his opinion a case of rupture of the stomach.

The mortality of our series was not really high considering the types of patients coming to the Hospital mostly walking or jolting in a gharry, 12 to 24 hours or even later after perforation.

As regards drainage of the peritoneal cavity it was not in favour of one unless in a late case there was a localised collection, but he thought it better to drain the wound in late cases. Local sulphonamides were not used and even according to the speaker and from other statistics, residual abscesses were more frequent in those where sulphonamides were used locally.

Dr E. Borges was glad that Dr Sen had laid great stress on adequate post-operative management as a factor in reducing mortality especially the need for intravenous fluids. He agreed with him that vitamin C was essential for wound healing and in the prevention of burst abdomen, but he would like to point out that even more important in this respect was correction of hypoproteinaemia which is mainly responsible for defective wound healing. Serum protein determinations were essential in the post-operative period and if the value was found to be less than 5 gms. per cent, plasma transfusions were essential.

He also enquired if there were any cases of perforation occurring while under observation in the wards in the series and how they had fared. He had the misfortune to see two such cases and had formed the opinion that these cases are usually diagnosed late and treated late as the usual rigidity is much later in appearance in cases receiving excellent medical care from the moment of perforation than in cases that perforate outside the hospital and are brought in a jolting conveyance.

Dr P. K. Sen replying to Dr Arthur DeSa agreed that the division of the case in five year periods for an assessment of results was a very good suggestion and also that radiography in doubtful cases was very valuable. As regards the differentiation between coronary thrombosis and acute peptic perforations, though on occasion this was difficult the low B.P. and the state of true shock in acute coronary occlusion that always develops should indicate the true state of affairs. An adlogram in such a case would prove very valuable. He agreed with Dr E. Borges that hypoproteinaemia played a most important part in wound healing and was possibly responsible for many burst abdomens, but he also stressed the importance of vitamin C administration in this connection preoperatively, in large doses intravenously. Vitamin C was well known to be directly responsible for collagen production from fibroblasts in tissue repair. Answering one of Dr Borges' questions he said that there were three cases which perforated while undergoing actual medical treatment in this series. All the three cases died even though the operation was done in all the three within the first six hours.

As regards the question raised by Dr T. O. Shah he said that the fact of rise in total number of cases of perforation in parallel with the total number of all cases admitted to the K. E. M. Hospital cannot be denied if one studies the two charts namely the yearly incidence of perforation and total yearly admissions of all cases. However he agreed with Dr Shah that the total number of cases of unperforated gastroduodenal ulcers must be taken into account. The use of falciform ligament in closing the perforation, he said was entirely free from the risks that Dr Shah feared. The ligament remains attached to the porta hepatis and the free and wrapped round the duodenum and virtually, it forms a further extension of the free outer edge of the gastrohepatic omentum thus there is never an actual free band in the peritoneal cavity. He agreed with Dr Shah who stressed the need of draining whenever in doubt contrary to the usual teaching.

In reply to Dr Munsiff who advocated the use of the Spencer & W. suture for burst abdomen, Dr Sen was of opinion that other methods of repair do equally well and the W. suture presented no special advantages. The local autohaemotherapy advocated by Dr Phadke Dr Sen said did not appear to be based on very firm ground. Blood, specially clotted blood is a very good medium for rapid bacterial growth and the immunity factors present in the small quantity of blood left in the peritoneal cavity are small. As such he did not advocate it as a routine measure. Local autohaemotherapy for other inflammatory lesions e.g. carbuncles have not stood the test of the time and he thought that the salutary results in the very few cases where this form of therapy was tried were merely incidental.

In reply to Dr Glinde's assertion that the mortality factors in the present series were not poor, Dr Sen said that though the large number of late cases in the present series were partly responsible for the high mortality, the figures were still not flattering and left plenty of room for improvement.

In conclusion Dr Sen said that though the "pointing sign" as described by him was not a classical test mentioned in literature, he had found it of great value and appealed to members present to put it to test in their own cases whenever possible.

Dr R. N. Cooper in his concluding remarks stated that the apparently large mortality of our operated cases to peptic ulcer perforations was due to the fact that a very large majority of the cases came too late for treatment. The lapse of time between the perforation and the surgical interference was the most important single factor influencing mortality statistics. In the present series on 24 cases out of 116 came to the hospital within 24 hours of the perforation. Another factor to be reckoned with was the undernourished condition of the patients who sought relief. Whereas in European countries the highest incidence of peptic ulceration was amongst the upper strata of life such as the lawyers, surgeons and "merchant princes", in our own country these cases were mostly drawn from the undernourished work people such as the bus-drivers, mill hands etc. The excellent figures shown in Russia were due to the fact that there were special facilities for the treatment of all emergency cases such as a separate emergency hospitals with the whole staff on rotational duty for full 24 hours.

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# BLOOD TRANSFUSION

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This form of medical treatment has been known from very olden times and it has been repeatedly taken up and dropped again. The Egyptian Pharaohs thought that blood was a strength-giving fluid and so they used to bathe their bodies with this life saving fluid obtained from their slaves and enemies. Obviously, it did not do them any good and so this practice was abandoned. This idea re-  
 • curred again at frequent intervals during historical times. Harvey's discovery of circulation of blood gave a good impetus to this form of treatment—of giving the blood directly into circulation and in 1665, a Cornish physician carried out blood transfusion from one animal to another. The first blood transfusion in human beings was done by Denys de Montpellier, Physician to Louis XIV. Shortly the treatment became unpopular and it was stopped everywhere—England, France and Rome. About 150 years later a Guy's Hospital Obstetrician again started this method and he could save many patients. It was a mere chance that his patients were saved. After a short period of popularity it was once again abandoned. Landsteiner shall ever be remembered for changing the whole practice of blood transfusion from a matter of pure chance to a controlled scientific procedure by a great discovery of the blood iso-agglutinins and iso-agglutinogens in the year 1900. From this, it came to be known that different people belong to different blood groups and that if one is transfused with the blood of a wrong group, the result might be disastrous—immediate death might result. R.B.Cs contain iso-agglutinogens and there are iso-agglutinins in the serum. When blood from two different persons is mixed, if iso-agglutinin comes in contact with particular iso-agglutininogen, the R.B.Cs will agglutinate. This agglutination if it takes place in circulation during a blood transfusion, the patient is likely to die suddenly. R.B.Cs contain two iso-agglutinogens A and B and the serum contains two corresponding iso-agglutinins  $\alpha$  and  $\beta$ . Human blood is divided into four groups classified by Moss as I, II, III and IV whereas the corresponding international classification is according to the presence of iso-agglutinogens in R.B.Cs viz., AB, A, B and O. Hemagglutination occurs whenever homologous agglutinin and agglutininogen are in contact, it being a necessary histological axiom that homologous agglutinin and agglutininogen cannot exist together in the same blood.

Moss	International.	Iso-agglutinogens in R.B.Cs	Iso agglutinins in plasma	Receive blood from	Give blood to
I	AB	AB	Nil	AB(A, B or O)	AB only
II	A	A	$\beta$	A(or O)	A(or AB)
III	B	B	$\alpha$	B(or O)	B(or AB)
IV	O	Nil	$\alpha \beta$	O only	O(AB, A or B)

The agglutinogens present in blood are stronger than the agglutinins and the agglutinins in the plasma of the transfused blood get very much diluted with the recipient's blood volume. From this it is clear that the real danger in giving a transfusion comes from the donor's corpuscles. If the recipient's serum contains any agglutinins, that is to say, if he is of group A, B, or O with serum containing  $\beta$ , agglutinins respectively the donor's corpuscles should not contain the corresponding agglutinin. Thus the person of group A can receive blood from group A or group O. Group AB serum contains no agglutinins and so he can be given any kind of blood. This group is therefore known as universal recipient. Group O R.B.Cs contain no agglutinogens and hence they can be given to persons of any blood group. This group is therefore known as universal donor. Donor's serum contains agglutinins which are weaker than agglutinogens. If blood is given slowly and not in large amounts, the serum will be diluted by recipient's blood and no agglutination of his red cells will occur. But if blood is given fast and in large amounts, the donor's serum may agglutinate the recipient's corpuscles. This danger applies when the universal donor gives blood to a person not of his own group or when the universal recipient receives blood from any group other than his own group. This danger is particularly to be afraid of when the agglutinins are present in high titre. A universal donor with agglutinins present in high titre is known as a dangerous universal donor and such donors should only be used to give blood to persons of their own group. It is essential therefore that direct cross-matching should always be done whenever a blood transfusion is to be done.

*Transfusion of conditioned universal blood*—The blood of dangerous universal donor (i.e., donor belonging to group "O" with agglutinins present in high titre) can be made safe by partial or complete neutralization of  $\alpha$  and  $\beta$  agglutinins which are present in the serum. This can be done by the addition of small amounts of purified A and B specific substances, which are available in recent years. Landsteiner found 'A' specific substance from horse saliva and Goebel obtained it from commercial peptones. Potent 'B' substance has been isolated from the gastric juice.

'A' (25 mgms) and 'B' (10 mgms) in physiologic solution of sodium chloride in 500 c.c. of "O" blood are injected into the blood in the vacuum container and mixed gently for a few minutes before giving a transfusion. Addition of these blood group specific substances to normal human serum containing the corresponding iso-agglutinins does not result in a precipitation.

*Determination of blood group*—This can be carried out by means of sera of groups A and B. If the corpuscles under the test are agglutinated by both sera, these corpuscles belong to A B group, if by group B serum only, they belong to group A, if by group A serum only they belong to group B, if by neither sera, they belong to group O. This method of determining a blood group is known as the indirect

test In the direct test, the serum of the recipient is tested against the corpuscles of the donor Ideally, both direct and indirect tests should be performed before giving a transfusion

*Intra-group agglutinins*—Repeated transfusions from the same donor sometimes produces a disastrous accident One explanation for this is that the donor's R.B.Cs contain an agglutinin which acts as an antigen and stimulates the formation of agglutinin This newly developed agglutinin is responsible for agglutinating the R B Cs which were quite compatible at the first transfusion This human corpuscular factor, capable of stimulating dangerous agglutinins, corresponds with one found in the R B Cs of rhesus monkeys—rhesus factor (Rh+) 85 per cent are Rh+ve and 15 per cent are Rh—ve Repeated transfusions from Rh+ve to Rh—ve are potentially dangerous This complication may arise even with a first transfusion in cases of pregnancy, before, during or soon after delivery This occurs when Rh—ve mother produces Rh+ve child through Rh+ve father and during pregnancy may develop anti-Rh agglutinins in response to the foetal agglutinin and even with the first transfusion R.B.Cs will agglutinate Ideally Rh—ve recipient should be transfused from Rh—ve donors especially during pregnancy

*Age and Blood Groups*—Agglutinogens are always demonstrable at birth The agglutinins that the child possesses at birth are derived from the mother by filtration through placenta Whatever agglutinins are present at birth, diminish in titre or disappear during the first ten days of life, after this new agglutinin appears This phenomenon is due to loss of maternal agglutinins followed by the production of the infant's own agglutinins There is thus no need to carry out cross matching tests before giving blood from the mother to an infant during the first week of its life

*Indications for Transfusion*—Transfusion is used to restore the volume of circulating blood and to contribute any deficient or missing element

1 *Acute Haemorrhage*—A loss of 2 pints or more of blood causes symptoms usually described as shock

The ideal fluid is fresh blood or stored blood, but any of the protein containing blood substitutes efficiently restore blood volume

2 *Reduction in R.B.Cs*—Chronic anaemias or anaemias found in septicaemia toxæmic states as typhoid and nutritional conditions such as ulcerative colitis etc, respond very well to repeated small transfusions

Fresh blood given by continuous slow drip technique in order to allow time for the circulation to adjust itself to the increased volume and to excrete the unwanted plasma portion Blood substitutes are useless Concentrated suspensions of R.B.Cs are particularly suitable for cases of aplastic anaemia

3 *Reduction in W.B.Cs*—Transfusion is useful in both primary or idiopathic agranulocytic angina and secondary agranulocytic angina

4. *Reduction in platelets*—Platelets supplied from a transfusion may tide over the acute phase of the essential thrombocytopaenia

5. *Haemoglobin Deficiency*—In cases of coal gas poisoning, the effective circulating haemoglobin is reduced by the formation of carboxy-haemoglobin. Venesection followed by transfusion is the ideal method of treatment

6. *Deficiency of other clotting elements*—Transfusion is sometimes very effective in checking haemorrhage in cases in haemophilia, obstructive jaundice, acute haemolytic anaemia of Lederer haemorrhagic disease of the new-born etc. Fresh blood is essential for such transfusion

7. *Wound and Burn Shock*—In these cases circulating blood becomes concentrated and viscosity puts a great load on the circulation. Whole blood if transfused may increase this embarrassment of circulation. Plasma or serum transfusion is indicated in these cases.

8. *To give immune bodies*—Specific immuno-transfusion can be carried out by immunizing the donor with a vaccine. This is advised in cases of infective endocarditis

9. *Cases of Peptic Ulcer* were successfully treated with repeated small intravenous injections of 34 cc of goat's blood. Heterogeneous transfusions have also been advised for tropical ulcers of skin and inflammatory joint lesions

*Stored Blood and Blood Substitutes*—Blood can be stored for as long as three to six weeks by adding a suitable anti-coagulant. Blood should be collected in a sterile manner and should be stored in the cold at 4°C. Freezing must be avoided otherwise haemolysis is rapid. The anti-coagulants that are used are sodium citrate solution, 10 cc of 3 per cent solution to be added to every 100 cc of blood, heparin, citrate sucrose & citrate dextrin mixtures and I.H.T. fluid (recommended by Moscow Blood Transfusion Institute). Blood conserved with a glucose citrate solution can be successfully kept in a condition suitable for transfusion for 25 days. The advantage of I.H.T. fluid is that it is used as equal parts with blood and the blood that is well diluted keeps well. Stored blood up to fourteen days' old equals fresh blood, so far as red cells are concerned, and that the reaction rate is no greater

*Plasma*—Blood is collected using sodium citrate as an anti-coagulant, and is then stored up in the cold room as above for a couple of days or so. The RBCs will settle down at the bottom of the bottle and the plasma is to be decanted off by a closed method. Plasma can be dried up and can be used in either normal strength or in a concentrated form if necessary by reconstituting the plasma in distilled water. It is very useful in the treatment of peripheral circulatory failure due to trauma, burns and haemorrhage where haemo-concentration contra-indicates the use of blood transfusion. Fluid plasma should be stored in the dark at room temperature. Refrigeration encourages clotting. It keeps for at least two years. Properly prepared plasma on standing may coagulate and form minute masses

of fibrin, potential emboli. All plasma therefore before being administered intravenously should be filtered. Another advantage of plasma transfusion is that by using "pooled plasma or serum", the need for blood grouping is eliminated. By 'pooled' plasma we mean plasma taken from the blood of a number of persons of different groups, that has been "pooled" in a large vessel. When blood of A group is mixed with that of B group  $\infty$  agglutinins in A blood will act with the B agglutinogens in B blood, and  $\propto$  agglutinins in B blood will act with A agglutinogens in A blood and agglutination of R.B.Cs will take place. As the R.B.Cs are not to be used, this does not matter. All the agglutinins in the plasma will be absorbed by the agglutinogens in R.B.Cs and the plasma will be safe for giving to a patient of any group.

*Blood Serum*—It is as effective as citrated plasma for blood volume restoration. Sterile blood serum is easier to prepare than citrated plasma. An objection to massive serum transfusion is that it tends to cause a high proportion of undesirable reactions. Like plasma, it can also be dried up and reconstituted in the desired strength according to the requirements. Fluid serum should be stored in the dark either at room temperature or in a refrigerator. It keeps for at least two years.

*Transfusion of Resuspended Corpuscles*—Kolmer recommends the transfusion of resuspended corpuscles remaining at the bottom after separation of plasma in suitable cases of anaemia. These red cells retain their full oxygen carrying capacity upto eight days. They are to be diluted with glucose saline. Reactions can be reduced by removing white layer on the top consisting of leucocytes and platelets and filtering the mixture before use.

*Auto-transfusion*—Reinfusion of blood shed into the peritoneal cavity was first practised by Thies of Leipzig in 1914, but as early as 1885 John Duncan of Royal Infirmary, Edinburgh, reinfused the blood which dripped from an amputated limb after adding sodium phosphate as an anti-coagulant.

Auto-transfusion is most commonly practised in cases of haemorrhage into one of the body cavities e.g. pleura in cases of traumatic haemothorax or peritoneal cavity in cases of ruptured ectopic or ruptured liver or spleen. Sometimes blood may also be collected from a viscus after its removal e.g., following splenectomy.

The blood may be collected by means of suction and is received into a sterile glass funnel lined with six or more thickness of gauze, muslin or fine mesh silk soaked in 3 per cent citrate. The reservoir should contain 3 per cent sodium citrate solution.

*Advantages of auto-transfusion are many*—No time is wasted in grouping or cross matching or in obtaining a donor. Risk of an incompatible transfusion or transmission of disease is eliminated although severe reactions may occur if old or contaminated blood is used.

Blood replacement should not be attempted if intra-peritoneal haemorrhage is of more than 24 hours' standing, if there is an associated bowel or other hollow viscus injury or if biliary apparatus has been damaged

*Placental Blood*—It differs considerably from the adult blood. It contains a higher per cent of haemoglobin (average 115 per cent), more R.B.Cs (average six millions) and more white cells (average 11,680). This requires 20 per cent dilution of the placental blood in physiologic salt solution. It is rich in gonadotropic and oestrogenic hormones and contains certain substances, which exert a powerful immunizing action on measles. 50-125 c.c. of blood may be obtained from each maternity case. Contamination can be avoided with a little care.

*Marrow Transfusion*—About 2-5 c.c. of fluid is withdrawn from sternal bone marrow of a suitable donor and is injected slowly into the sternal cavity of cases of aplastic anaemia, purpura, pernicious anaemia etc.

*Other Blood Substitutes*—Trial has been made of isinglass 0.5 to 1.0 per cent solution of pectin and ox albumin. None of these products nor purified human albumin have passed the experimental stage.

#### *Technique of Transfusion and Precautionary Measures —*

*Selection of Donors*—The donors should be young and healthy between the ages of twenty and thirty. Transmissible diseases like malaria and syphilis must be excluded. Donors with a definitely allergic history should be avoided. A homologous donor should be preferred to a group O universal donor. Both indirect and direct tests for compatibility should be performed. This is of great importance in the case of repeated transfusions to the same recipient of Rh-ve group. The risk of transmission of syphilis lies in cases in which whole blood is used immediately or stored whole blood is used early. The Wassermann reaction cannot entirely eliminate this risk. There might be cases (1) in which the person tested is incubating the disease and (2) in which a chancre is present but in an early sero-negative stage. If the blood of such a donor is stored at 4°C for about four days, it can be given without any danger of contracting transfusion syphilis. Some workers used mapharsen to rid infected citrated blood of *treponema pallidum*. They found that 0.01 gm. per 500 c.c. of citrated blood was amply sufficient. Mapharsen is of low toxicity and in the amount suggested, the dose is so small as to be most unlikely to affect even a seriously ill person. It may be contraindicated when the recipient is suffering from haemorrhagic purpura, exfoliative dermatitis, or hepatic and renal diseases.

Bacterial contamination in stored plasma can be prevented by proper aseptic measures. The addition of 0.2 per cent of a sulfonamide derivative, preferably sodium sulfathiazole, actually sterilizes minimally contaminated specimens regardless of the organism or the temperature involved (4°-24°C).

**Selection of Fluid.**—The selection of the fluid for transfusion depends upon the condition of the patient. In order to give fresh blood or stored blood, not used, all other elements—leucocytes, etc.—necessitate fresh blood. For renal stored blood or one of the blood substitutes there is haemoconcentration e.g., in renal states there is haemoconcentration e.g., in renal states fluid of choice in haemorrhagic conditions. Citrated blood is the method of choice as it is easily manipulated. For given intravenous injection of 1 mgm of weight Transfusion should be started in and should be completed in about thirty minutes the coagulation time of the donor's blood, and Defibrinated blood is rarely used as the process of defibrination removes the vital elements and the blood is usually toxic unless it is given within a few hours.

There are two methods of giving a transfusion—the indirect—the latter is more extensively used. In the indirect method the blood is given directly from the donor to the recipient by way of a syringe whereas in indirect method, the blood is given from a donor in a flask containing a suitable anti-coagulant then given to a recipient either immediately or after storage. Workers advise to warm the blood to body temperature before giving it, whereas others give cold blood as it comes from a storage flask.

## ROUTES OF ADMINISTRATION

**Sub-cutaneous and Intra-muscular**—This is advised in cases of haemorrhagic disease of the new born, in various stages of the disease, auto-haemo, in some of the infectious fevers during the convalescent stage from a convalescent patient, in some cases of anaemia. There is no need of typing or cross matching the blood given by this route. About 10-20 cc or more is given at a time.

**Intravenous**—This is the commonest route. If the veins are not seen, the blood can be given in the upper arm after doing a fontanelle puncture. The veins of the lower arm are sometimes more suitable than those of the upper arm. If the veins are not visible, they can be dissected out and used.

**In the Marrow**—The blood can be given in the marrow after doing a sternal puncture or tibial puncture. This method is sometimes very useful when the patient is very flabby plethoric individuals.

**Rate of Transfusion**—Klauffe and DeBakey give 650 cc of blood in 3 minutes without endangering the cardio-vascular system. This rapid rate is a saving measure e.g., in acute haemorrhage. If the shock is present, transfusion should be given rapidly.



Kekwick have laid down four cardinal principles for transfusion of severely anaemic subjects (1) Rate not to exceed 1 c.c. per lb. of body weight per hour (2) If haemoglobin is 25 per cent or less and if there is cachexia or cardiac or respiratory disease, rate should not exceed 0.5 c.c. per lb. of body weight per hour (3) Maintain steadily the determined rate and do not accelerate for short periods (4) If dyspnoea, cough or basal rales appear, suspend transfusion

A reasonable rate of transfusion in chronic anaemia is 40 drops per minute and giving of one pint of whole blood should be spread over at least three hours, if disasters from circulatory overloading are to be avoided

*Complications of Blood Transfusion*—Appreciation of the dangers attending the practice of blood transfusion has varied greatly at different times. In the seventeenth century a happy ignorance took no account of them whatever. In the eighteenth century, they were so greatly feared that transfusion fell into abeyance. In the nineteenth, it was realized that dangers existed but they were imperfectly understood. From the beginning of twentieth century, with the discovery of "blood group" it has become a controlled scientific procedure from a matter of pure chance.

*Simple pyrexial reactions*—Foreign protein, contained in improperly distilled water, improperly prepared solutions and dirty apparatus is the commonest cause of these reactions. Pyrexia and rigors are also common with transfusion of over-age blood, infected blood and incompatible blood. Too fast a rate of administration of blood sometimes causes a rigor, which rapidly subsides if the rate be slowed. *Treatment* when the rigor occurs, is to suspend the transfusion, give hot water bottle and inject  $\frac{1}{2}$  c.c. of 1 in 1000 solution of adrenaline. If the rigor is very severe, not relieved by these measures, inject morphine gr  $\frac{1}{4}$  with atropine  $\frac{1}{50}$  gr. It will shorten the attack, relieve the right heart and quieten the anxious patient. It will also prevent excessive pulmonary and bronchial secretions which may so quickly collect and drown the patient.

*Allergic Reactions and Urticaria*.—If the donor has any allergic history, e.g., hay fever, and is in the active phase at the time of transfusion, he may transmit this tendency to the recipient. These reactions are usually mild and unassociated with any marked constitutional symptoms and are usually accompanied by a varying degree of urticaria and eosinophilia. They occur especially with repeated transfusions using the same donor. Allergic reactions may be minimised by making the donor fast for some hours before the transfusion.

*Haemolytic Reactions*.—These may occur not only when the blood introduced is of an incorrect group, but also when donor and recipient are of the same blood group. The clinical features are the same in both the cases but they are less marked when the blood introduced is of the correct group. Intra-vascular haemolysis may occur apart from the wrong grouping in the following cases (1) On re-transfu-

sion, (ii) when universal donor is used to give blood to a patient of different group, and (iii) in transfusing the haemolytic anaemias like acholuric familial jaundice. The clinical features of this condition are severe pain in the loin, rigor, respiratory embarrassment, circulatory collapse, haemoglobinuria, haemalbuminaemia etc. Those who survive the immediate haemolytic shock, get renal failure in terminal stages as a result of deposition of haematin pigment in the renal tubules. Some workers ascribe renal failure to damage caused to the kidney by arterial spasm and ischaemia.

*Pulmonary Oedema and Cardiac Failure*—These complications occur in patients suffering from heart disease or long standing anaemia. The rate and volume of transfusion should be properly regulated as mentioned before.

*Transmission of Diseases*—Syphilis, malaria, etc. may be transmitted to the recipient if the donor is suffering from them. In the donors these diseases may be latent clinically. So proper precautions should be taken to prevent these diseases in the recipient.

Blood transfusion is a life-saving measure in some cases and every medical man should be familiar with its technique. Any medical man can give a transfusion successfully after proper precautions and no elaborate apparatus is essential for this purpose. Physicians and surgeons, gynaecologists and obstetricians—all are quite familiar with the good results they get in their practice by the help of this measure. Some of the major operations, which the surgeons were very much afraid to perform, are successfully carried out after the introduction of this therapeutic measure. Anaesthetists do not find the same difficulties as they used to find before transfusion came in and anaesthesia work has also become much easier. It is therefore essential that this measure should be very extensively used and all the benefits should be given to the suffering humanity. Blood banks should be established all over the country and the blood should be easily available for any one at an insignificant cost.

#### ONION PASTE AS A DRESSING

(Continued from p. 41)

has to be made immediately before use. The preparation consists simply of grinding the peeled onions or a portion of it and then placing the paste into a glass dish with a diameter equal to that of the wound. This is applied so that the paste does not come in contact with the wound, which is exposed only to the onion vapour for ten minutes. Of 11 patients treated, seven had amputations of the arm, one of the thigh and three of the foot, and all the wounds showed distinct purulent inflammation before treatment. After the first phytoncide treatment, the doctors report, all the wounds without exception became rose-coloured and the patients no longer complained of pain. After the second treatment much of purulence and odour subsided. After five days all the cases showed extensive soft epithelialization. The Soviet scientists feel that phytoncides have a place in the treatment of infected wounds along with synthetic preparations such as the sulpha drugs.

# Critical Notes and Abstracts

## PAREGORIC AS AN EXPECTORANT

Laboratory investigations carried out by E M Boyd and M L MacLachlan (Canadian Medical Association Journal, April, 1944, 50-338) provide data confirming the high clinical reputation which paregoric (comphorated tincture of opium, B.P) has had as an expectorant for at least two centuries. Using a method based upon measurement of the output of respiratory tract fluid, which has been elaborated for the investigation of expectorants, they found that in all the animals investigated, which included cats, rabbits, guinea-pigs, hens, and albino rats, paregoric produced an increased volume of respiratory tract fluid, varying from 28 to 331 per cent. They also found that this effect was annulled by a section of the afferent vagal fibres from the stomach, thus suggesting that the expectorant action of paregoric is due to a reflex initiated through the stomach. Whilst each of the individual constituents of paregoric (i.e., tincture of opium, camphor, benzoic acid, oil of anise, and alcohol) produced an increased volume of respiratory tract fluid, the summation of the effects of the individual ingredients was not so great as when they were combined, as in paregoric. This synergistic action was only obtained with preparations of paregoric that were at least one year old, fresher preparations having a much less marked effect. On standing for long periods paregoric develops a dark brown colour, as compared with the pale, light brown colour of fresher preparations, and it is this dark brown preparation that is most effective. Whether some interaction occurs over a period of time between the individual ingredients that is responsible both for this darkening in colour and the enhanced expectorant action is a problem still awaiting solution. As these experiments have produced such consistent results in a large variety of animals, it is probable that their results can be applied to man, thus justifying the use of this old therapeutic measure in the treatment of dry, hacking coughs, provided preparations of paregoric that have been matured for at least two or three years are used in preference to fresher preparations.

## ONION PASTE AS A DRESSING

According to Medical News Letter No 38, issued by the United States Office of War Information, promising results with onion paste used as a dressing for infected wounds have been reported by Dr I. V. Toroptsey and Dr A. G. Filatova, of the Tomsk State University and the All-Union Institute of Experimental Medicine, USSR. The experiments with onion paste followed reports by Dr B. Tokin, that the essential oils of onion, garlic and certain other strong-scented vegetables contain substances that kill bacteria, protozoa and even larger organisms. These substances, or phytoncides, have not yet been identified chemically, but are extremely volatile, so that the paste

# Reflections & aphorisms

## TEACHING OF MEDICINE

There is now, and always has been, great diversity of opinion with regard to the methods which should be pursued in the teaching of medicine. This is reflected in the great variety of texts now available. The text most popular with the student is the one which follows a conventional outline, which furnishes him the essential facts required for the passing of his examinations, and which serves as a ready reference in the solution of a specific medical problem. Such texts, no doubt, fill a need. Nevertheless, the mere accumulation of facts, however valuable they may be in actual practice, cannot be regarded as an ideal form of education. The student who is interested in acquiring only immediately useful facts becomes a sort of tradesman or artisan actuated by the viewpoint that his sole obligation is to treat disease—the particular disease which a patient may happen to present. He is not likely to see his patient as a complex, integrated organism whose many functions are intimately co-ordinated, inter-related, and interdependent. Neither does he see the patient in relation to the environment, and therefore cannot realize that illness is often the result of a long series of social and economic maladjustments, hereditary tendencies, insanitary conditions, vicious habits, or educational neglect.

Another defect in the form of education based on the accumulation of unsorted, poorly understood factual data is that it inevitably leads to atrophy of the critical faculties. How much more satisfying it would be to the young physician, if, in his all-too-short a period of training, he could find time to study medicine as it has slowly evolved, and thus learn really to understand the relation of medicine to the growth of civilisation. For one thing, he would realize that there are few medical "discoveries" but that rather our present knowledge represents the cumulative experience of many generations of priests, physicians, physicists and philosophers, the painstaking study and observations of many centuries. For another thing, he would gain a better insight into the obligations he assumed on becoming a member of the profession. Lastly, he could hardly fail to sharpen his critical faculties while acquiring habits of thinking and study and this would result in his becoming a man of wide interests and broad vision and, eventually, perhaps in his becoming an educated physician.

The presentation of necessary factual matter in medical education should not be neglected, but greater emphasis should be placed on understanding than on memorizing. At the same time every effort must be made to arouse the interest of the student, in the hope that an aroused interest will lead to further investigation. Any emotional reaction that is produced in the student, except that of fear, should be regarded as desirable.

W. H. HOLMES

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# The Indian Physician

VOL IV NO 3

MARCH 1945

WHOLE NO 39

## Original Contributions

### THE AZYGOS LOBE OF THE LUNG

#### ACCESSORY LOBE OF THE AZYGOS VEIN

By

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(With 9 figures)

Raman (1944) reviewed the literature on azygos lobe of the lung, discussed its aetiology and reported two cases. Since the publication of this paper five more cases were observed and further search of the literature has revealed larger number of cases. From the available literature a complete list of cases recorded by various observers from the first anatomical description of the condition by Wrisberg in 1778, is now given in table I.

In the earlier years upto 1923 the condition was described by the anatomists. Afterwards the condition was diagnosed by routine radiological examination (Wessler and Jaches 1923) which later on was confirmed in some cases by post-mortem (Bendick and Wessler 1928).

The following is a brief summary of the five additional cases observed by the author in the King George Hospital, Vizagapatam.

(1) Hindu male, K R aged 30 years, admitted on 4-1-44 for pain in the precordium. Routine radiological examination for the heart revealed the azygos lobe of the lung on the right side (Type B of Stibbe). This case was further investigated by injection of lipiodol. This was done through the bronchoscope in the first branch of the right bronchus. The roentgenograms did not show any evidence of lipiodol entering into the azygos lobe (Figs 1 and 2). It is possible that the lipiodol injected might have gone little further missing the small branch that supplies the azygos lobe. The meso-azygos deviated to the right at the level of the middle of the fourth dorsal vertebra.

(2) European male, S C aged 34 years came with a history of bronchitis. Routine radiological examination of the chest on 17-1-44 showed the azygos lobe of the lung of the right side (Type B of Stibbe) (Fig 3). The meso-azygos deviated towards the right at the level of the lower end of the fourth dorsal vertebra.

(3) P B R Hindu male, aged 12 years, was admitted on 12-11-44 for rheumatic heart disease with congestive heart failure. Radiogram taken for the heart on 17-11-44 showed not only evidence of rheumatic heart disease but in addition revealed azygos lobe of the right lung (Type B of Stibbe) (Fig 4). The meso-azygos deviated towards the right at the level of the lower border of the fourth dorsal vertebra.

The relations of this patient were investigated radiologically for evidence of azygos lobe (6 males, 3 females).

(1) Father aged 36 years, (2) Mother aged 28 years, (3) Brother aged 5 years, (4) Sister aged 3 years, (5) Maternal uncle of the patient aged 50 years, (6) Son of maternal uncle aged 16 years, (7) Son of

TABLE I

	No of cases	Barsony & Koppenstein	One or two per week
1778 Wrisberg (Anatomy)	1		
1870 Chene (Anatomy)	1	Hepner	1
1899 Fischer	1	Macknull	1
1903 Poirier & Sharpy (condition is described)	?	D'Hourand Fertin	?
1919 Stibbe (Anatomy)	23		35+?
1923 Calrney (Anatomy)	2	1931 Levy and Cade	6
Wessley & Jaches	?	Meurdelles & Jalet	15
	2+?	Nelson and Simon	4
		Casrelli	1
1927 Velde	5	Brule and Lhuere	1
Muller (Radiograph & Post mortem)	1+?	Brown and Braverman	1
	6+?	Shannan	4
			34
1928 Bendick & Wessler	50	1932 Oroz	7
Mathar & Coope	4	Arlabosse	0
Hjelm & Hulten	13	Bourdellez and Jalet	?
Swess	1		18+?
Neumann	4	1933 Cockrayne	2
	72	Vita	1
1929 Emil	3	Bottaliga	3
Illing	13	Underwood and Tattersall	12
Keliser	10		18
Minchert	13	1938 Choussat	1
Litten	0		
Stoloff	6	1944 Raman	2
Lesser	12	Viswanathan	2
Hamish	11	1945 Raman (present series)	5
Beevaz	5		0
	79		
1930 Jalet	16		
Volmer	10		
Muller & Weber	6		
Kayne	1		
		Total	205+?

maternal uncle aged 13 years, (8) Daughter of maternal uncle aged 10 years, (9) Son of maternal uncle aged 5 years

None of them showed the azygos lobe of the lung or any other congenital abnormality

(4) P V R Hindu male, aged 25 years, was admitted on 11-1-45 for chronic bronchitis and emphysema of the lung. On radiological examination of the chest, azygos lobe of the right lung was found (Type B of Stibbe) (Fig 5). The meso-azygos deviated to the right at the level of the middle of the fifth dorsal vertebra. He had only one male relation, i.e., father living. He was radiologically investigated but did not show this congenital abnormality.

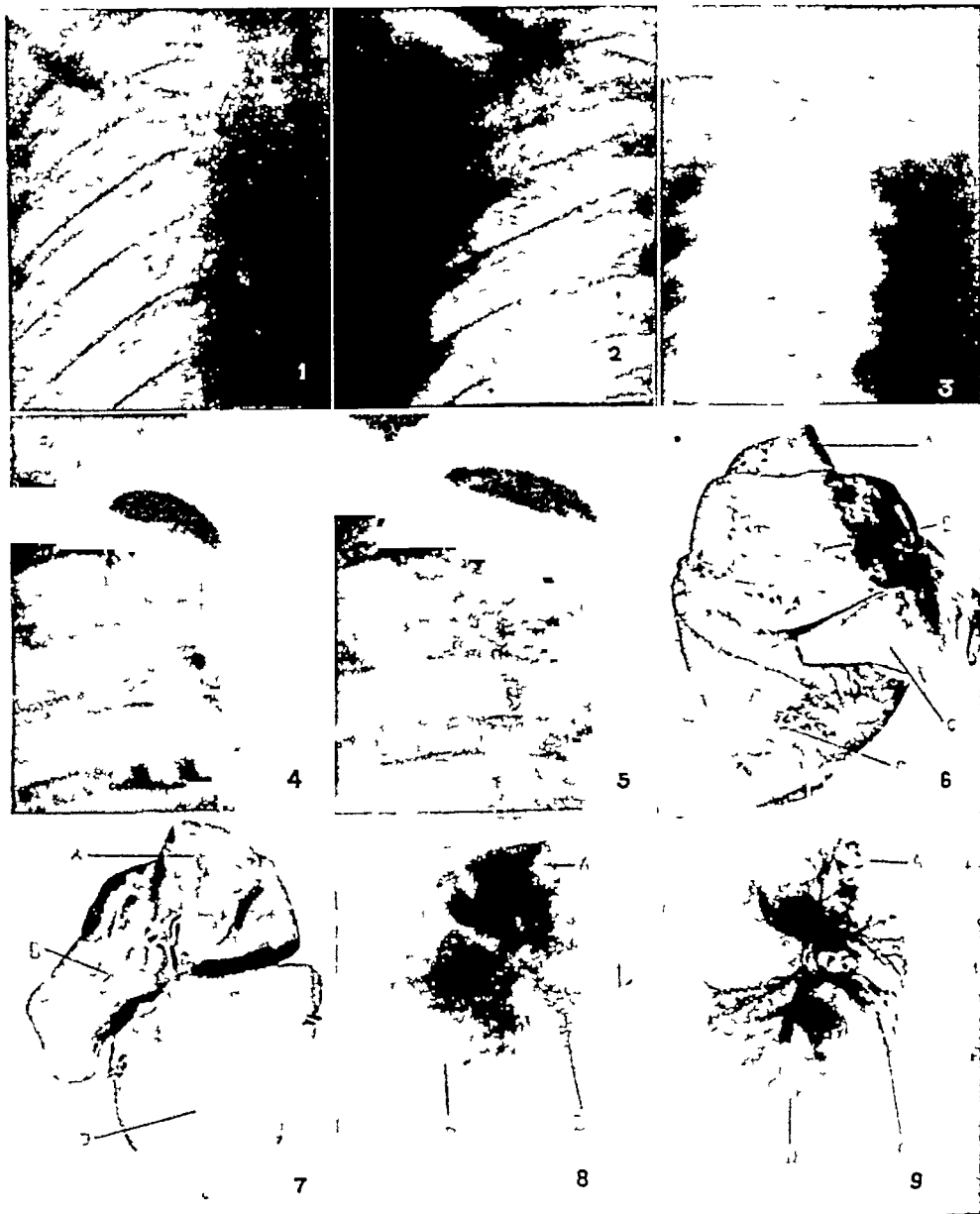


Fig 1 (Case 1) showing the azygos lobe of the right lung (Type B of Stille)

Fig 2 (Case 1) showing that the lipiodol did not enter the azygos lobe

Fig 3 (Case 2) showing the azygos lobe of the right lung (Type B of Stille)

Fig 4 (Case 3) showing the azygos lobe of the right lung (Type B of Stille)

Fig 5 (Case 4) showing the azygos lobe of the right lung (Type B of Stille)

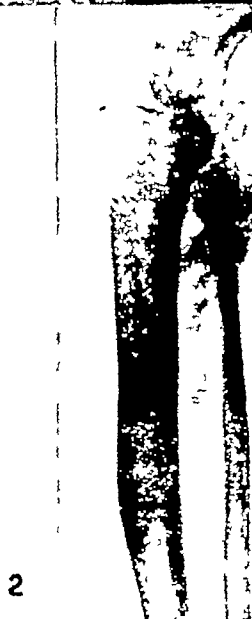
Fig 6 (Case 5) Photograph of the post mortem specimen (antero-lateral view) of right lung showing all the four lobes (A) azygos lobe (B) upper lobe (C) middle lobe (D) lower lobe

Fig 7 (Case 5) same post mortem specimen as above (posterior medial view) showing (A) azygos lobe prominently (B) upper lobe (D) lower lobe Middle lobe is not visualised in this picture

Fig 8 (Case 5) Radiogram of the post mortem specimen showing different lobes (A) (B) and (D) (C) is not clearly visualised The letters correspond to the same lobes as in figs. 6 & 7

Fig 9 (Case 5) Radiogram of the post mortem specimen of the lung in which lipiodol has been injected showing the lipiodol in the azygos lobe (A) very prominently and that this branch is derived from the eparterial bronchus (B) and (D) same lobes as above injected with lipiodol





For description, see text on pp 50 51 and 52

(5) K D Hindu male, aged 30 years, was admitted on 7-6-44 with a history of fever of 10 days' duration. Physical examination showed jaundice, enlarged spleen and liver and pneumonia of the left base. The condition of the patient gradually became worse and he died on 11-6-44. A post-mortem conducted on 16-6-44 showed jaundice, enlarged spleen, enlarged liver and congestion of all the organs. The left lung weighed 48 ozs and showed congestion and suppuration of the lower lobe due to lobar pneumonia. Right lung weighed 24 ozs showed azygos lobe (Type B of Stibbe) (Figs 6 and 7). Measurements of the azygos lobe were Length 3 in, breadth 2.1 in, thickness 1.6 in. The depth of the fissure reached the level of the hilum. Lipiodol injected into the post-mortem specimen (Figs 8 and 9) showed that the bronchus of the azygos lobe was derived from the eparterial bronchus. Lipiodol in this case did not enter the middle lobe. But a subsequent picture taken with additional lipiodol injection showed that it has entered the middle lobe.

Abstracts of all the seven cases of azygos lobe of the lung are given below in a tabulated form in table II.

TABLE II

Date	Name	Age	Sex	Type after Stibbe	Level of deviation of meso azygos to the right
1 4-1-44	K.R	30	Male	B	Middle of the fourth dorsal vertebra
2 17 1-44	S.C.	34		B	Lower end of fourth dorsal vertebra
3 7 11 44	P.B.R	12	,	B	Lower end of fourth dorsal vertebra.
4 13 1-45	P.V.R	25	,	B	Middle of the fifth dorsal vertebra
5 10-0-44	K.D	30	,	B	The diagnosis was made by post mortem. The fissure reached the level of the hilum
*6 8-4-43	J.R	28	„	Between B & C	The azygos vein and the lower end of the meso azygos are obscured by pleural effusion. The upper end assumes a triangular shape called commissural triangle (Levy and Cade) or Triangle of Implantation (D'Hourand Fertin)
*7 29 7 43	G.N	30	„	„	Lower end of the fourth dorsal vertebra

\* Previously reported (Raman 1944)

## DISCUSSION

All the cases were in males, one in a European and the other six in Indians. The youngest was 12 and the oldest 34 years of age. Six belonged to (Stibbe Type B) and the seventh intermediate between type B and type C, nearer C than B. Cairney (1923) in one of his cases showed that eparterial bronchus divides into two main branches viz (1) horizontal and (2) vertical. Two of the vertical branches were directed towards the main apex and the third supplied the accessory lobe of the azygos vein. Bendick and Wessler (1928) demonstrated by injecting the bronchus of a lung removed post-mortem, that the azygos lobe was supplied by a small branch from the eparterial bronchus. In case 5, under review, lipiodol injection of the post-mortem specimen showed that a branch from eparterial bronchus supplied the azygos lobe.

The measurements of the azygos lobe in two cases of Cairney (loc cit) were as follows

	Length	Breadth	Thickness
(1)	3 "	1½"	1¼"
(2)	1¾"	1¼"	¾"

In case 5 of this series the measurements were as follows

Length	Breadth	Thickness
3"	2 1"	1 6"

In the first case of the present series (K R 30 years) the lipiodol introduced through the bronchoscope did not enter the azygos lobe. It is possible that the lipiodol might not have entered the small vertical bronchus supplying the azygos lobe.

Underwood and Tattersall (1933) suggested heredity as an aetiological factor. In one of their cases, seven of a family of ten were examined radiologically and one case was recognised. Three members of a family of another case revealed one more. Of the seven cases seen by the author one had no children and his other relations were far away. The relations of four could not be had for a routine radiological examination. Nine relations of one case (No 3) and the only one surviving relation of case (No 4) were examined radiologically but showed no evidence of azygos lobe.

#### SUMMARY

1 Further search of literature has shown a total number of over 290 cases of azygos lobe of the lung.

2 Five more cases of azygos lobe of the right lung, four diagnosed radiologically and the other by post-mortem, are described.

3 Lipiodol injected during life in one case did not enter the azygos lobe.

Lipiodol injected into the post-mortem specimen showed that the bronchus supplying the azygos lobe was derived from the eparterial bronchus.

4 Radiological examination of nine relations of one patient and one of another did not reveal the azygos lobe.

*Acknowledgment*—The author's thanks are due to Dr. B. Tirumala Rao for the lipiodol injection in case 1, to Dr. C. Benjamin for the radiograms and to Dr. T. Bhaskara Menon for the post-mortem of case 5.

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# HEMANGIOMATA

## AND SIMILAR DISEASES OF THE BONES ESPECIALLY OF THE LIMBS

By

DOZENT Dr GEORGE POLITZER

( From the Princess Surendra Kumari Memorial Central X Ray Institute, Pabala )

( With 5 figures )

The hemangioma of the bone is a rare disease, mainly localised in the vertebræ and the convexity of the skull. The changes in the vertebræ which are considered as pathognomonic are described as follows. The structure of the body of the vertebra becomes "grobwabig und strähnig" (honeycombed and skeiny) and the concave circumference of the body gets straight or even convex. The observations on which these diagnostic features are based are entirely correct but it happens rather seldom that the above symptoms are observed *in vivo*.

As for the structure it must be kept in mind that the X-rays depict the vertebra after a passage through the whole diameter of the trunk and finer details of the structure are usually effaced under these conditions even in spite of the use of modern apparatuses and the Potter-Bucky diaphragm. What we see is usually hardly to be distinguished from an ordinary porosis or rarefaction. As for the contour of the body the change of the concavity into convexity is only rarely recognisable because the vertebra usually collapses before these changes have properly developed. If once such a fracture has occurred, even the structural details can no more be made out, as the compression changes the condition of the spongiosa entirely. The isolated porosis of the body of one vertebra only is surely rather suspicious for the presence of an angioma but it is not pathognomonic, because this symptom appears in other diseases also.

It may be remembered that usually tuberculosis of the vertebra is localised near the upper or lower terminal plate, so that at the time of the first clinical symptoms the primary focus has already broken through the intervertebral disc and affected the terminal plate of the adjacent vertebra too. But in rare cases the primary focus lies in the centre of the vertebra and then the first radiological symptom to be observed is a porosis of the body of the vertebra hardly much different from that observed in cases of angioma. The differential diagnosis between these two diseases is well illustrated by Fig 1. As far as the vertebra is concerned the porosis lacks any typical features, but on both sides of the vertebra a soft tissue shadow is visible which bulges towards the adjacent lung tissue. These convex soft tissue shadows prove beyond doubt that Fig 1 represents a case of tuberculosis and not of angioma. Another difficulty in the diagnosis of the angiomata of the bones lies in the fact that they are usually discovered but accidentally and rather late, as there are no early clinical symptoms. It

is superfluous to publish here a picture of the typical angioma of the vertebræ as these are contained in all bigger manuals of radiodiagnosics of the diseases of bones and joints. Also the angioma of the convexity of the skull is well known. It leads to a localised swelling of the calvaria and to the appearance of mostly radial bone trabeculæ grouping themselves round the centre of the affection. There is hardly any difficulty in distinguishing these angiomas from the periosteal sarcoma of the skull because the latter starts from the outer cortex, while the angiomas begin in the diploe. But nearly unknown is the symptomatology of the hemangioma of the bones of the limbs so that a description of its main features is essential in view of the serious mistakes we encounter occasionally. Fig 2 shows an X-ray picture of the lower leg. The tibia contains a clear central spot with sharp polycystic outlines. The capsule of this central cavity is thick and dense and it looks like suspended into the surrounding spongiosa by solid radial bone strands. There exists no similar picture in any other bone disease but the central bone-angioma. It is astonishing that repeatedly these pictures are mistaken for sarcomata as shown by the following report:

When I was a scientific collaborator of the Central X-ray Institute of Prof. Holzkecht in Vienna, I used to show interesting bone pictures thrice a week to the Post-graduates of the American Medical Association of Vienna. When I demonstrated once the case published in Fig 2, an American physician working in the morning in another hospital in Vienna got up and said that a similar case had been seen by him that very morning and that the radiologist of the hospital had diagnosed it to be an osteo-sarcoma. The surgeon called in for the inspection of the picture decided to amputate the leg the same day. The American physician left my lecture immediately to get the operation stopped if possible, but he returned only with the amputated leg. This sad event permitted us not only to take fresh X-ray pictures of the case but to control by macro- and microscopical examination of the bone the correctness of the interpretation of the above symptoms. It may be noted also that contrary to the condition in the spine the tendency to spontaneous fracture of bones of the limbs affected with central angioma is very small. In the large material which I was able to observe so far, not a single case of spontaneous fracture of an angioma of the bone of a limb has been observed.

A second group of affections of blood vessels which manifest themselves in changes of the bones are the aneurysmata. The changes of the spine in cases of aneurysmatic dilatations of the thoracic aorta are well-known. There is a flat groove extending over several vertebræ which forms a bed wherein the aneurysma lies. As the thoracic aorta lies left to the spine the best pictures are obtained in the first oblique diameter (fencers position). In these pictures we see clearly that the outline of the groove is sharp and that the compacta of the body has not diminished in thickness inspite of the erosion. This is usually explained by the assumption that due to the slow retraction of the

bone following the influence of the pulsations of the aorta the osteoclastic processes on the surface of the vertebra are combined and compensated by osteoplastic processes leading to the transformation of spongiosa into compacta in the depth of the groove. While this picture is well known similar processes in the limbs did not find any attention so far. Fig 3 shows the lower leg of an adult. The first impression will be that the lower end of the tibia contains a big cyst as if a giant cell tumour. But at closer inspection the strange polycystic formation lies neither in the tibia nor in the fibula but between both. Especially in the upper end of the abnormal zone we see clearly that there are sharply outlined superficial grooves while the compacta is not diminished in size and thickness but only bulging into the marrow space. Distally the picture becomes a bit more complicated due to the complexity and superposition of the various part-erosions. The case corresponds to an aneurysma of the interosseal artery with erosion of the adjacent bones. These cases are not often to be found but there is not the smallest difficulty to arrive at the correct diagnosis if the picture, especially the upper and lower end of the affected area, is properly analysed.

There is a group of changes of the soft tissues and the bones which are due to angiomata. Fig 4 shows a lateral view of the area of the knee joint. The soft tissue contains a sponge-like shadow of great density. It consists of a meshwork of densely calcified bone wherein various small clear spaces are visible. One or the other of these spaces has regular circle shaped outlines as the result of a cylindrical canal being represented by the X-rays in the direction of its axis. These shadows concern primarily the soft tissues only but in more advanced stages they reach the bones or are fused with them as if in the case of Fig 5. There are even cases where the same sponge-like structure can be followed into the bone and sometimes we gain even the impression that they are penetrating the bone and leaving it on another side of its surface. These cases correspond to hemangiomata racemosa where the interstitial tissue has undergone a complete and compact ossification. The cases are not all too rare and it is rather essential that the diagnosis is made by the radiologist, because a surgical interference in these cases leads to severe bleeding which can hardly be stopped. On the other hand the disease is harmless except for some local pains caused by the piercing of the soft tissues by the pointed ends of the ossified bodies. I have never observed any spontaneous fracture of a bone in subsequence to this affection. There are hardly any differential diagnostic difficulties, if the clear round spaces in the calcified area are properly studied. Especially the circle shaped ones amidst them are extremely characteristic. It has already been explained above in which way their apparition is to be explained.

It has been described in which way diseases of the blood vessels are affecting the skeleton. I purposely refrain from a report about the cases in which aneurysmata can be discovered by the calcification of their walls and from a description of the different diseases in which

the walls of the blood vessels are impacted with lime These processes have no direct bearing to the bones themselves

Concluding it can be said

1 The angioma of the vertebræ shows only seldom the features which have been described as pathognomonic The differential diagnosis between these angiomata and the central tuberculosis of the vertebral body is discussed (Fig 1)

2 The typical features of the central angioma of the tube shaped bones of the limbs have been described (Fig 2)

3 Aneurysmata of peripheral arteries show principally the same erosions of adjacent bones as known from the condition of the spine in cases of aneurysm of the aorta (Fig 3)

4 The typical symptoms of the angioma racemosum with ossification of the interstitial tissue have been outlined and represented (Figs 4 and 5)

(For figures see plate facing page 47)



# Society Proceedings

## STABWOUND OF THE HEART

Dr K M Shah, M S (Bom) A Hindu male, aged 25 years, was admitted for a stab wound in the chest inflicted about four hours ago. He was in a state of collapse with a feeble pulse beating at the rate of 140 per minute. There was a stab wound in the fourth left intercostal space, by the side of the sternum, 1 inch in length and half an inch in breadth and going deep to the intercostal muscles, with blood pouring out in a constant stream. There was a pneumothorax with surgical emphysema on the left side. The clinical picture suggested cardiac tamponade, and an immediate operation was decided upon. The 4th and 5th costal cartilages with a part of the sternum were removed and the tear in the pericardium was exposed. The tear in the pericardium was an inch in length, it was extended and the tear in the heart, a quarter of an inch in length, was laid bare. After an anchoring suture, through the apex of the heart, the tear in the heart muscle was sutured with four interrupted stitches. A pleuropericardial fistula was made to drain the pericardial cavity, which was closed with interrupted sutures. The patient made an uneventful recovery, with a residual thickened pleura.

## INJURY TO THE FEMORAL ARTERY

Dr K M Shah, M S (Bom) A Hindu male, aged 35 years, was admitted for a small punctured wound in the middle of the left Hunter's canal from which he was bleeding profusely. Pulsations of the dorsalis pedis and the posterior tibial arteries were very feeble, whereas in the radials they were normal. On exploration of the wound the bleeding was profuse and on exposing the femoral artery it was found to be cut in 7/8th of its circumference and a small bit of iron particle was found underneath the tear. As the general condition of the patient did not permit an arterial anastomosis, ligature with excision of the artery was done, the foreign body was removed and the wound closed in layers without a drainage. After the operation the patient complained of severe pain in the calf muscles and tingling, numbness and loss of sensations in the leg which were relieved by intravenous administration of 100 c cm of 5 per cent sodium chloride, and continuous ice packs to the limb for 72 hours. On the third day after operation feeble pulsations were felt in the posterior tibial and on the fourth day in the dorsalis pedis. 10 c cm of 1 per cent novocaine were injected in the 2nd, 3rd and 4th lumbar sympathetic ganglia on the fifth day after operation because of recurrence of severe pain in the calf, which was later relieved. As the pain recurred again, two days later, 4 c cm of absolute alcohol were injected into 2nd, 3rd, and 4th lumbar sympathetic ganglia on the 9th day, and immediate and lasting relief was obtained. The patient is taking Buerger's exercises regularly and is now fully recovered except for a little coldness of the affected limb.

Cases presented before the 43rd Meeting of the G S Medical College and K E M Hospital Staff Society Bombay, on November 18, 1944, with Dr R N Cooper, F R C S in the Chair

# *Report of the Clinical Conferences*

AT THE TATA MEMORIAL HOSPITAL, BOMBAY

Conf on 6 10-44

## CARCINOMA OF THE CERVIX

A case of Carcinoma of the Cervix with distant metastasis presented by **Dr J C Paymaster** († 5269) He said that the biopsy report on the above case was anaplastic epidermoid carcinoma grade III The patient was given a full course of radiation, completing her treatment in December, 1943 She kept well for nine months About a month ago she came with a history of pain in the right side of the chest and a swelling in the left parotid region The x-ray picture of the chest revealed destructive lesion of the 10th rib on the right side suggesting metastatic deposits Aspiration biopsy of the left parotid stated presence of malignant tumour cells This case was presented as being a rare case showing metastatic deposits from cancer of the cervix in a distant organ such as parotid Reviewing the literature Dr Paymaster said that remote metastasis from cancer of the cervix occurred only in 30 per cent of the cases Leitch found visceral metastasis in 25 per cent of the autopsy examinations Liver was involved in 8 per cent of cases Lungs and peritoneum in only 4 per cent of cases Secondary deposits in the tubes and ovaries occurred in only 1 per cent of cervical cancers Warren reviewing the autopsies of 300 cases of the cancer of the cervix stated that bone metastasis occurred only in 4 per cent of cases In discussion **Dr V R Khanolkar** suggested a formal biopsy from the rib metastasis

## CYLINDROMA OF THE SUBMAXILLARY GLAND

A case of Cylindroma of the Submaxillary Gland presented by **Dr D R Meher-Homji** († 8065) A Hindu male of 38 years old, with a history of swelling in the right submaxillary region of 10 years' duration In 1938 this swelling was excised at Vengurla It recurred 8 months after the operation and increased in size to reach the present stage of the swelling It measured 6 x 6 x 5 inches and occupied the entire right upper neck The swelling was nodular at places and fixed to the deeper structures Consistency of the swelling was hard at places and definitely fluctuating at other places The swelling could be felt in the floor of the mouth and had pushed the right lateral pharyngeal wall inwards Clinical diagnosis of mixed salivary gland tumour was made and the patient was admitted to the hospital for investigation X-ray of the right mandible revealed a smooth walled defect in horizontal ramus Biopsy of the tumour was reported as cylindroma As regards treatment it was decided to remove the entire tumour mass with the removal of the mandible on that side after ligation of external carotid artery on that side

**Dr Meher-Homji** also presented a case († 8140) of a 40 year old Muslim female with the history that 6 years ago she was operated for

a tumour of the right breast and right radical mastectomy had been performed About 15 years ago she was operated for bleeding per vaginum and had a subumbilical median incision of a previous operation She noticed a mass in the left breast of 6 months' duration She stopped menstruating 6 months ago but previous to that her periods were profuse Physical examination revealed a large firm mass in the outer quadrant of left breast with hard nodes in the left axilla Pelvic examination revealed a marked smooth enlargement of the uterus, together with a small smooth mass in the left broad ligament Clinical diagnosis of carcinoma of the left breast with left axillary metastasis with fibroid of the uterus was made The case was presented in order to discuss whether the left breast tumour was primary or secondary to the right breast tumour The opinion was that the breast tumour was primary and that the histological diagnosis of right breast tumour was doubtful

#### ABDOMINO PERINEAL RESECTION OF THE RECTUM

A patient after abdomino-perineal resection of the rectum was demonstrated by **Dr E J Borges** († 7680) A 45 year old man with a history of painful defecation of one year's duration He had a proliferating growth at the anal margin involving the adjacent skin and involving the rectum for 4 cms above the anus No palpable metastasis in the groin or elsewhere A biopsy showed a squamous carcinoma grade II It was decided to do an abdomino-perineal resection rather than the limited perineal resection because a part of the rectum was involved An exploratory laparotomy was done through a left rectus incision, the condition was found operable and a Lahey first stage operation completed with a terminal colostomy in the original incision and implantation of the distal part into a suprapubic stab incision On 1-9-44 the second stage was done and the recto-sigmoid mobilised through a subumbilical midline incision and removed finally from the usual perineal approach One feature about this case that was remarkable was that the patient had a B P of 80/60 He received 950 cc of blood and 450 cc plasma during the operation The pulse kept under 100 throughout the operation, and the patient gave no anxiety afterwards **Dr Borges** said that the problem of urinary infection had been minimised but by no means solved by drugs like mandelic acid and cibazol and measures like tidal bladder drainage He suggested a modification of the first stage which appeared advisable to all the members of the surgical staff, viz, the implantation of the terminal colostomy loop into a stab incision in the left iliac region rather than into the original rectus incision This removes the colostomy from the proximity of the subumbilical incision in the second stage and prevents contamination in the post-operative period **Dr B N Surcar** commented on the fact that although the B P and the pulse were good indications about the patient's condition in most cases he had from his experience come to rely more on the state of the patient's skin in assessing the onset of shock As long as the skin was

dry and not moist and clammy all was well with the patient. He also pointed out the dangers of spinal anaesthesia in this operation.

#### CANCER OF THE THYROID

A case of bone metastasis in Cancer of the Thyroid was shown by **Dr E J Borges** († 8150). A 45 year old Muslim came with a painful swelling in the right iliac bone of a 1½ year's duration. There was a globular swelling on the right iliac crest which pulsated. This suggested a thyroid metastasis and the patient was made to uncover a goitre which he had hidden so far. This goitre he said was there from his childhood and he did not want anything to be done about it. On examination the thyroid presented the usual appearance of a colloid goitre of about 3 times the size of the normal thyroid. Careful palpation revealed hardness localised to the posterior aspect of the left lobe which felt like calcification. This was probably the site of carcinomatous change. **Dr Borges** pointed out that this case and a few others which were seen at this hospital were a lesson that might well be brought home to physicians who are in the habit of advising against surgery in persistent thyroid swellings. In answer to **Dr Athle** he said that the incidence of malignancy in colloid goitre was 1 per cent. The incidence of malignancy in an adenoma of the thyroid was over 80 per cent. A discussion about the treatment of this case followed and it was decided to have a biopsy of the tumour for record and follow this with deep X-rays to the metastasis as the patient was unwilling to have anything done to his goitre. **Dr Khanolkar** mentioned that it was sometimes found that the removal of the primary carcinoma in the thyroid was followed by a regression of the metastasis and occasionally removal of the metastasis as well cured the patient.

*Conf on 13 10-44*

#### METASTATIC DEPOSIT IN BONE

**Dr J C Paymaster** presented a case († 7792) of a man of 43 who complained of pain in the lumbar region. The only positive finding in the history was an attack of pleurisy 3 months ago. He had been treated outside as a case of Pott's disease but as the pain was not relieved by usual methods he was referred here for further investigations. An X-ray diagnosis of metastatic deposit was made and he was treated with deep therapy with great relief of pain. Subsequently he developed haemoptysis and pain in the shoulder. **Dr L H Athle** discussing the X-ray diagnosis said that a careful examination revealed the presence of a pathological fracture. There was definite evidence of bone destruction in the body. This excluded a simple fracture or Kummel's disease. Tuberculosis was excluded because of lack of the usual findings. Primary bone tumours were rare in this location and none of them would fit in with the appearances. He concluded therefore that a secondary deposit in the body from an undetected primary source was the only possible diagnosis. Subsequent appearance of haemoptysis and another deposit in the scapula supported the view that a small bronchogenic carcinoma was responsible for the lesion.

## METASTATIC DEPOSIT IN BONE

**Dr E J Borges** showed a 60 year old man who had developed a painful lump in the back of 2 months' duration († 8222) The swelling was hard and definitely in connection with the thoracic wall **Dr Athle** demonstrated the destructive lesion involving the vertebral ends of 3 ribs There was no new bone formation The chest was otherwise clear His diagnosis of metastatic carcinoma was proved by aspiration biopsy from the mass

**Dr E J Borges** showed a young man of 20 who had noticed a swelling of his chest wall for about 5 months († 8166) A hard oval swelling in connection with the 7th and 8th ribs could be clinically made out **Dr Athle** discussed the radiograms showing a large soft tissue mass arising from and replacing the distal half of one of the ribs Flakes of new bone were seen inside the mass A chondroma or chondrosarcoma was the most likely possibility He favoured the latter because of the rapid growth and destruction of part of the rib **Dr Sirsat** discussed the biopsy and opined that it was a case of chondrosarcoma **Dr Mody** suggested that in view of the marked resistance of these tumours to radiation, surgical treatment should be given

## CARCINOMA OF THE BASE OF THE TONGUE

**Dr K P Mody** described the history of a case († 3384) of carcinoma of the base of the tongue The primary site did not show any evidence of disease after a full course of deep X-ray therapy Some months later a node appeared in the upper cervical region This was treated by radon seeds and subsided, soon to be followed by another node above the treated area While she was under X-ray treatment for this a chest examination demonstrated the presence of metastases A question had been raised if the radium or X-ray treatment was in any way responsible for the dissemination to the lungs He was convinced that there was no connection between the two but he welcomed a full discussion on the question

**Dr Athle** remarked that the dramatic appearance of distant metastasis during or soon after radiation therapy in a few cases is so impressive that some people are tempted to establish a cause and effect relationship between the two This idea was not new As early as 1927 Hunter made a statement that radiation provoked metastasis by his observation of a single case of breast cancer treated by radium Generalised metastases were seen soon after the treatment of the primary Bell and Datnow made similar suggestions after treating 2 cases of cancer of the cervix by radium implantation The American Journal of Cancer refuted these ideas in an editorial in 1930 The question can be examined from the clinical point of view Firstly metastases are a natural development in the course of cancer in the human body Latent metastases may exist prior to the surgical and radiation therapy Subsequent detection should not be confused with the spread of cancer after the treatment For example many cases of cancer of the breast came back with metastatic deposits in various organs soon after a

mastectomy The operation cannot be said to have provoked metastasis The same applies to radiation therapy The clinical studies at cancer institutions where a large number of cases are treated by radiation therapy do not show any significant increase in the number of distant metastases when compared with the figure of untreated cases or cases treated by surgery The slight increase in the percentages of distant metastasis is due to the prolongation of life of cancer-bearing patients due to the control of the primary growth Metastases have a chance to grow because the primary growth itself does not endanger life A few of our larynx cases have lived to 2 or 3 years without any disease in the throat and then developed visceral metastases Untreated these would not have lived for more than a year and would have possibly died because of the primary growth itself Cancer of the cervix patients ordinarily die of infection or renal complications Control of the primary at least enables them to live long enough so that a few of them show distant metastasis Jeanneney found no significant increase of distant metastasis in the autopsies he had performed on treated cases of cancer of the cervix On the experimental side sufficiently controlled work has not been done regarding this problem Sugarbaker, of Memorial Hospital, New York injected India Ink before irradiation and found that there was no increased acceleration of the ink particles in the lymph channels From this he concluded that the radiation does not affect the passage of the cancer cells to distant areas Studies of radiated tumours at various stages of treatment do not show any increase in the presence of cancer cells in the lymph or blood channels Dr Athle concluded by saying that planned experimental work with tumour bearing mice will settle this problem once for all He himself based his opinion that radiation does not provoke metastasis, on the strength of the enormous clinical evidence which was available for any one to study Dr V R Khanolkar felt that more precise work should be done on this problem There were many lacunae in our knowledge of the exact process of the spread of tumours We must direct our efforts towards understanding of the relationship and reactions between the growth and the tissue in which it grows

Conf on 20 10-44

#### INTRAFASCIAL FIBROMA

Dr M. V Sirsat presented a specimen of intrafascial fibroma removed at operation from a Muslim aged 45 († 7797) who complained of a large swelling in the left thigh of 2 years' duration The swelling had been rapidly growing for the last 6 months It was firm to feel and slightly fluctuating The tumour was excised. It measured 12 x 10 x 6 cms and showed on cut section an area of necrosis in the centre and at the periphery were seen interlacing strands of connective tissue The microscopical examination of the section from the periphery of the tumour showed a typical structure of a fibroma The interesting feature of the specimen was a marked degree of central necrosis

## SQUAMOUS CARCINOMA FINGER

The second specimen presented by Dr Sirsat was an amputated left finger from a male radiologist aged 41 years (D 472) who worked in the X-ray department continuously for 10½ years. The nature of his work was screening and developing of films. A hard scab-like growth appeared on the terminal phalanx of the left ring finger 5 years previously but since 6 months became worst and a raw wound appeared since a month. The X-ray showed an evidence of bone destruction without any bone proliferation in the terminal and middle phalanges. The specimen showed at the terminal phalanx a greyish cauliflower-like tumour mass which on cut section showed an erosion of the underlying bone. The histological examination of the section from the growth showed Squamous Carcinoma grade I.

## RHABDOMYOSARCOMA OF THE TONGUE

A case of Rhabdomyosarcoma of the tongue presented by Dr J C Paymaster († 7344). He said that this patient was a female of 58 years. She came to the hospital with an ulcerating growth in the region of the right tonsil, base of the tongue and right gingivo-lingual gutter. The growth was fleshy and bled easily on touch. The duration of the symptoms was only 3 months. Enlarged neck nodes on the right side. An emergency ligation of the right external carotid was done on 10-7-44. The patient later developed large neck nodes on the right side. She also complained of pain in the sacral region. She was treated by X-rays for the oral lesion and the sacral metastasis. The lesion did not regress with radiation. She gradually became worse and died. Dr V V Gharpure discussed the histopathology of this case. He said that the histological examination of the sections showed a diffuse hyperplasia of large polygonal and ovoid cells. The cells showed a good deal of variation in size and shape. The cells had a faintly basophilic cytoplasm and large round and ovoid pale nuclei. Presence of 1 to 2 prominent nucleoli, presence of frequent atypical mitosis and a fair number of tumour giant cells. With an oil immersion lens one could see faint striations in the cytoplasm of a few cells. Diagnosis Rhabdomyosarcoma.

## LEIOMYOSARCOMA IN THE TONSILLAR AREA

Dr D J Jussawalla presented a case of Leiomyosarcoma in the tonsillar area († 8088). He said that the patient was a Muslim male of 60 years. He complained of a sore in the region of the left tonsillar area since the last 15 days. History of pain in the same area for the last 20 days. On examination there was found a fungating growth 5 cms in diameter in the left tonsillar area involving the soft palate and the anterior pillar. After a course of deep X-rays he removed the tumour as much as he could. Dr V V Gharpure discussed the histopathology of this case. He said that the histological examination showed intertwining bundles and whorls of ovoid and fusiform cells. The cells varied in size and shape. The cells have a basophilic cytoplasm and large ovoid nuclei with rounded ends. Presence of frequent atypical

mitosis **Diagnosis** Leiomyosarcoma In referring to the literature on this subject he said that there are few records of rhabdomyosarcoma and fibromyxosarcoma of the tongue In the tonsillar area the commonest type of sarcoma was a lymphosarcoma Other types of sarcomas if at all they occurred were very rare **Dr D J Jussawalla** asked as to from which tissue the leiomyosarcoma had started **Dr V R Khanolkar** said that it was not necessary to assume that it started from a particular tissue in that area but it could arise from mesenchymal cells which had a pleuripotential capacity for development

#### DENDRITIC ADENOCARCINOMA OF SUB MAXILLARY GLAND

**Dr V R Khanolkar** presented a specimen of dendritic adenocarcinoma of Sub-maxillary gland († 8099) A piece of tissue was received in the laboratory on 28th of August, 1944, from the Salvation Army, Emery Hospital, Anand The accompanying note stated that it was a piece from a tumour of the neck which had been removed from a Hindu male 50 years old The clinical diagnosis was "mixed tumour of the sub-maxillary gland" It was also stated that the tumour had been present for several years in the patient but had been increasing in size lately The tissue had a greyish appearance on cut surface, dotted with numerous small cavities giving it a fenestrated appearance On microscopical examination it showed papillary protuberances and tubular or round acini lined by one or more layers of columnar epithelium In the core of the papillae and separating the tumour acini were strands of connective tissue The tumour cells had a faintly basophilic cytoplasm The nuclei were hyperchromatic and showed a variability in size and shape There were numerous sub-nuclear vacuolar areas situated in the lining epithelium, suggesting mucin secreting glandular tubules In view of the histology the following remarks were sent to the doctor "The histology is suggestive of metastatic deposit of a carcinoma It is suggested that the gastrointestinal tract may be investigated in this case roentgenologically In the absence of a tumour in this region a possibility of a primary at another site should be looked for We will be interested to learn from you the result of your investigations in this case"

In view of these remarks the case was referred to us and the patient presented himself for examination and treatment on 26th of September, 1944 **Dr D R Meher-Homji**, who studied the case described the clinical findings In view of the clinical, X-ray and laboratory examinations the slides were reviewed again and the literature on the subject studied further It was found that Chevassue had described a dendritic adenocarcinoma arising in the ducts, in which very numerous papillae were lined by multiple layers of cubical or cylindrical cells The tumour had promptly recurred after operation and had grown rapidly In the present case also there is evidence of a recurrence in 4 months



## Critical Notes and Abstracts

**RENAL DAMAGE FROM SULFONAMIDE COMPOUNDS** —Shortly after the sulfonamide compounds came into general use, physicians recognized that the kidney may be damaged in the course of therapy with these drugs. Two types of renal complications were observed: (1) those due to mechanical obstruction of the pelvis, the ureters and the renal tubules by crystals of the sulfonamide compounds and (2) those due to toxic lesions of the kidney without obstruction. Combination of the two forms has likewise been described. In addition to tubular necrosis, which is the usual expression of damage by toxic substances, instances were observed in which interstitial tissue reaction with necrosis was also present. Murphy and his associates<sup>1</sup> observed 1 such instance in the series reported by them. They feel that this type of reaction is probably an expression of severe idiosyncrasy on the part of the renal tissue to the drug. This inflammatory response was also seen in tissues outside of the kidney represented by giant cells and perivascular granuloma-like cell accumulations suggesting a similarity with periarteritis nodosa and similar lesions. The hepatic damage observed in these cases is probably related to the nephrotic complications.

Study of the clinical data of 14 patients with renal insufficiency following use of sulfonamide compounds in relation to post-mortem observations on 13 revealed that the quantity of the sulfonamide compound administered and the drug level in the blood appeared to be unimportant in producing the renal damage. As much as 41 grams and as little as 0.6 gram was responsible for fatal renal injury. In a few of their cases deposits of crystals of the drugs in the urinary tract causing some degree of mechanical obstruction were found associated with the nephrotoxic lesion, this was not the rule, however, as in most of the cases the nephrotoxic lesions were independent of mechanical blocking. Microscopic alterations in tubular epithelium were observed all the way from simple degeneration to tubular necrosis and intense inflammatory reaction outside the nephron. The investigators feel that these tubular lesions represent degrees in the severity of one process rather than different kinds of response. The study failed to correlate the clinical features with the specific site for the renal tubular damage.

Of the numerous toxic complications caused by sulfonamide compounds, that affecting the kidney is most serious. Fortunately these complications are comparatively uncommon. The mechanical type of complication, particularly that outside the kidney, in the pelvis and the ureter, responds best to therapeutic measures. When, however,

1 (J A M A 126 Sept 30 1944 page 3023) Murphy, Francis D. Muzma, Joseph F. Polley, Theodore Z., and Grill John. Clinicopathologic studies of Renal Damage due to Sulfonamide compounds, Arch Int Med. 73 433 (June) 1944.)

obstruction occurs within the kidney a cure is not easily accomplished, although always retrograde lavage should be done and the drug discontinued. Precipitation of the sulfonamide compound is the etiologic factor in these obstructions. Precipitation should be prevented as far as possible by the administration of adequate fluids and maintenance of an alkaline urine.

**THE EFFECTS OF HEAT**—Experience of the effects of heat on board ship are recorded by MacLean (1943). Muscular cramps were the outstanding feature. Only one patient developed hyper-pyrexia. The cramps were accompanied by headache, vomiting, vertigo and rapid, panting respirations, with, in most cases, a normal temperature. Cramps are due to loss of chlorides from excessive sweating, so that administration of salt was the basis of treatment, two teaspoonsful of salt in two pints of water being sipped during every twenty-four hours, in addition to 8 pints of sweetened fluid to which a teaspoonful of sodium bicarbonate was added. Rectal or intravenous salines were substituted when vomiting was severe. Preventive measures before entering the danger zone are necessary, as ship's water contains little or no sodium chloride; those advised were—

- (1) Add 1 lb of salt to the distilled water for every 350 men
- (2) All ratings to take half a teaspoonful of salt in a pint of water before going on watch
- (3) To take a teaspoonful of salt in a pint of water immediately on feeling the slightest symptoms, e.g. nausea, headache or vertigo

In contrast to this, the effects of land heat in Persia and Iraq are set out in a useful official memorandum (1943). The exogenous etiological factors were high humidity (a wet bulb temperature of 83° F being the danger point), rapid dehydration, lack of salt and of rest, endogenous factors were non-acclimatization, alcoholism, and especially illness associated with fever, vomiting or diarrhoea. The effects of heat are classified as—

- (a) Heat exhaustion—Common, but not usually serious, takes the form of a faint with a tendency to heat cramps
- (b) Subacute manifestations—Important, with insidious onset consisting of a pyrexial period of increasing derangement of body chemistry, with a final phase of high temperature, the symptoms being lassitude, headache, nausea and vomiting, insomnia and frequency. Chlorides in the urine are diminished. The condition lasts a week or so and requires treatment if disaster is to be averted
- (c) Acute heatstroke—Sudden failure of the heat mechanism in an apparently healthy person, with loss of consciousness, delirium, coma or convulsion. The skin is dry, the temperature may reach 112° F. The face is congested and the muscles rigid. The cerebro-spinal fluid is normal, but should not be rapidly withdrawn or death may result from pressure on the medulla

In treatment the essentials are a cool atmosphere, rest, replacement of fluid and salt, and reduction of the body temperature by physical means. Cooling measures must be stopped when the body temperature reaches  $102^{\circ}\text{F}$  (from  $106^{\circ}\text{F}$ ) or  $104^{\circ}\text{F}$  (from  $109^{\circ}\text{F}$ ). Anti-pyretic drugs are dangerous. Large quantities of fluid in the form of 0.25 per cent saline drinks must be given, or intravenous saline if the blood pressure be below 100 mm Hg. A balance sheet should be kept of fluid intake and output, allowing a loss of at least 8 pints per day as sweat. Intravenous administration requires care lest pulmonary oedema be induced. If there be doubt as to the presence of malaria, 8 to 10 grains of quinine should be given slowly, intravenously. A daily ration of  $\frac{3}{4}$  oz of salt should be taken before entering the heatstroke areas. In the hot season a minimum daily fluid requirement is 10 pints. A useful quantitative test for urinary chlorides is —

To 10 drops of a twenty-four hour specimen of urine add one drop of 20 per cent potassium chromate solution, this gives a canary yellow colour. A 2.9 per cent solution of silver nitrate is now added drop by drop until the colour changes to brown. The number of drops of the nitrate solution required equals the amount of sodium chloride present in grammes per litre (*The Practitioner*, Vol CLIII, November 1944, Pages 265-266).

**PRICKLY HEAT** — A minor scourge of hot climates is prickly heat which in Eritrea has been classified into five types (Bloomfield, 1943) —

- (1) The miliary or common form
- (2) Multiple boils and painful blisters on fingers, beginning as deep-seated swellings
- (3) Impetiginous rash, a concomitant of the common rash found on the alae nasi and chin
- (4) Pemphigous form, in which symmetrical crops of painful blebs and bullae filled with thin pus appear in the axillae and groins
- (5) Secondary fungus infection of the pemphigous lesions, in which the bullae become angry-looking pustules with black centres

Prickly heat is considered due to dys-function of the sweat glands from overaction, leading to blocked ducts followed by swelling with congestion and rupture of the gland capillaries, dysfunction of the smaller glands causing the miliary rash, and of the larger glands the pemphigoid condition. Other varieties are due to secondary infections. The name "climatic hyperidrosis" is suggested. Treatment demands minimal sweating, minimum of clothes, scrupulous cleanliness and constant towelling to mop up the sweat. Restricted fluid intake and a diet adequate in fresh foods is advised. A lotion of zinc oxide 30 gm, menthol 2 gm, alcohol 160 ccm, water 400 ccm, as used by the Italians, is comforting (*The Practitioner* Nov 1944, Vol CLIII, Pages 266-267).

# Reflections & Aphorisms

WHAT W S THAYER LEARNT FROM WILLIAM OSLER

¶Respect your profession and your colleagues Hold your tongue!

¶Do not allow yourself to laugh lightly and to jest on medical subjects in the presence of laymen You would not speak thus of your mother Hold your tongue!

¶Do not allow yourself to enter into controversies on medical subjects with un-understanding people, it is useless and futile and will often deliver you and your cause into the hands of your opponents

¶Every man, says Sir Thomas Browne, is not a proper Champion for Truth, nor fit to take up the Gauntlet in the cause of Veritie Many from an ignorance of these Maxims, and an inconsiderate Zeal unto Truth, have too rashly charged the troops of error, and remaine as Trophees unto the Enemies of Truth, a Man may be in as just possession of Truth as of a City, and yet be forced to surrender, 'tis therefore far better to enjoy her with peace, than to hazard her on a battle, Hold your tongue!

¶Never speak ill of a colleague If he seem to you to have done wrong, if you disapprove of his actions, show it by avoiding him if you will, but hold your tongue! Nine times out of ten you will find there are explanations for his action of which you know nothing If you speak, you become his enemy You can no more associate with him and remain an honest man Is it worthwhile?

¶Respect your colleague Close your ears Do not allow others to speak ill of your colleague in your presence Generally they are mistaken Remember that most doctors are honest men and decent fellows, even if you don't understand them Hold your tongue!

¶There is nothing that poisons the mind like the spoken and repeated word The reiterated word, be it true or false, becomes ere long a conviction, alike to him who speaks it and to him who listens

¶Beware the power of the spoken and repeated word! The Christian Scientists know it The German General Staff knew it, it was and is the whole story of their propaganda at home and abroad An assertion, an accusation, a suspicion, repeated and reiterated, soon becomes a conviction Hold your tongue!

¶Idle gossip, careless criticism may injure your neighbour, it always poisons you

¶Be simple Be yourself Don't "pronounce" In the newspapers most doctors "pronounce," which means that too many of us come to deceive ourselves and believe in our own omniscience Omniscience may not be a crime, it is a serious foible

¶Remember how little you know Don't be afraid to say you don't know Don't lay claim to superior knowledge

¶Don't judge your neighbour Too often the ill you think of him is but the reflection of your own faults "My son," says Marco to Guido, "each man sees in another individual that which he sees in himself, and each one comprehends that other individual in a different fashion, and precisely from the level of his own moral nature"

¶Don't take yourself too seriously Don't carry a chip on your shoulder There is nothing so pathetic or so funny as a doctor with a chip on his shoulder Too often it turns out to be a millstone You are dealing with ill difficult, often unreasonable people, but they are free agents You have no divine right to prescribe to them a code of ethics Their actions may disappoint you They may pain you Never let them offend you A wise man has said, "A cad is one who, when he is not giving offence, is taking it, and a properly behaved person never feels insulted because he never need" If you are capable of taking offence and feeling insulted at what your patients do, there is something the matter with you You have lowered yourself to the level of your unreasonable patient If a patient wants to leave you and go to your colleague, he has a perfect right to do so Help him and encourage him to do it if need be If he has lost faith in you or doesn't like you, you can't help him You have no God-given proprietorship in your patients They are their own masters Send them on their way with your blessing, 'tis the surest way to get them back

¶Commune freely and frankly and openly with your colleagues Mingle with them in societies Seek their aid Trust them in emergencies, and in the immense majority of instances they will merit your trust

¶Medicine is a jealous mistress You can serve her only with your whole heart Leave her if you will, but don't attempt to divide your allegiance with rivals, religion, art, politics, however alluring or worthy they may seem in themselves

¶The master word in medicine is work

# The Indian Physician

VOL IV NO 4

APRIL 1945

WHOLE NO 40

## Original Contributions

### A STUDY OF GASTRIC ACIDITY IN DISEASE

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Of all the constituents of the gastric contents which interest the clinician, the acid secreted by the stomach has already been considered as the most important. At first, attempts were made only to detect the presence of free hydrochloric acid and with this view various indicators were employed such as congo-red, Boas' reagent, methyl violet, Toepfer's reagent, etc.

It soon became apparent, however, that quantitative estimations of acidity were essential. It is difficult to say just when the titrimetric method was first employed in clinical gastric studies, but in 1886 Jaworski and Gluzinski introduced the present practice of estimating acidity in clinical units. They titrated the specimen with 0.1 normal alkali using litmus as an indicator. The proper choice of indicators, however, was a matter of great controversy. With the introduction of pH concept of acidity in 1909 by Sorenson, it became possible to define end points in terms of pH units. For free hydrochloric acid the accepted standard of end point is at pH 2.8, which is indicated by a salmon-pink colour with Toepfer's indicator. For total acidity the accepted standard of the end point of titration is from pH 8 to 10, which is indicated by the pink colour with phenolphthalein. Toepfer's reagent and phenolphthalein are used more extensively to-day than any other combination of indicators for routine clinical purpose.

When it was established that gastric analysis was useful as an aid to diagnosis of many gastric complaints, clinical pathologists tried to ascertain the cellular elements which were responsible for the secretion and the nature of chemical reaction or reactions by which hydrochloric acid is produced in the stomach. The histological elements responsible for secretion of acid juice are believed to be the parietal cells of the gastric glands. This is assumed on the basis of the fact that the regions in which these cells are chiefly present—that is the middle region of the stomach—the secretion is definitely acid and where they are absent or scanty in number, the secretion is alkaline.

The work was carried out under the direction of Dr V. R. Khanolkar, the Director of Laboratories.

Various chemical theories have been put forward to explain the formation of hydrochloric acid in the stomach. Three important theories are given below.

1 Hydrochloric acid may be liberated by hydrolysis of the chloride of weak base such as ammonia,  $\text{NH}_4\text{Cl} + \text{H}_2\text{O} \rightarrow \text{NH}_4\text{OH} + \text{HCl}$ . Ammonia is absorbed by gastric mucosa, liberating free hydrochloric acid in the stomach.

2 Hydrochloric acid is formed by the interaction of sodium chloride with acid phosphate,  $\text{NaCl} + \text{NaH}_2\text{PO}_4 \rightarrow \text{HCl} + \text{Na}_2\text{HPO}_4$ . This reaction is followed by  $\text{Na}_2\text{HPO}_4 + \text{H}_2\text{CO}_3 \rightarrow \text{NaH}_2\text{PO}_4 + \text{NaHCO}_3$ . Acid phosphate may thus be used again and bicarbonate is removed by the blood stream.

3 Sodium chloride may react with carbonic acid liberating free hydrochloric acid  $\text{NaCl} + \text{H}_2\text{CO}_3 \rightarrow \text{HCl} + \text{NaHCO}_3$ . This reaction has been carried out experimentally in the presence of protein.

Investigations were carried out by Pollard and Bloomfield (1931), Vanzant and Alvarez (1932), Davies and James (1930), and others to ascertain the nature of normal acidity curve of gastric juice. In India MacCay (1918) was the first to carry out some studies on this subject. S. L. Bhatia et al (1931) analysed the gastric secretion of 30 normal subjects, (17 non-vegetarian and 13 vegetarian) in Bombay. The main object of the study was to establish standard curve for normal Indians and to note the effect of diet on gastric secretion. No marked difference in gastric secretion was observed in the two groups. The average free hydrochloric acid content in all 30 normals was 20.23 cc and average total hydrochloric acid was found to be 30.95 cc. Maximum free hydrochloric acid as well as maximum total hydrochloric acid was 58 cc and 90 cc respectively.

L. E. Napier and C. R. Das Gupta (1941) established the following criteria for classifying acid curves according to the highest free acid readings, per 100 cc of gastric juice.

1	Achlorhydria	0
2	Hypochlorhydria	Less than 10
3	Isochlorhydria low	10 to less than 25
4	Isochlorhydria medium	25 to 45
5	Isochlorhydria high	45 to 65
6	Hyperchlorhydria	greater than 65

They found that above 80 per cent of normal individuals fall within the isochlorhydria range. Mangalik et al (1942) studied the gastric acidity curves in 161 normal individuals in U.P. and compared them with those obtained by L. E. Napier and others. He found that the acid response in Indians in U.P. shows no immediate fall in acidity after alcohol test meal and gives higher maximum rise as compared with that in Bengalis.

It has been found that the normal gastric acidity curve is different from that obtained in patients with duodenal ulcer, peptic ulcer or cancer of the stomach. In pernicious anemia and diabetes mellitus the curve of acidity is also different from normal.

L. E. Napier et al (loc cit) had studied fractional gastric analysis, with alcohol as test-meal, in 259 hospital patients suffering from a

number of different diseases. They found that the highest incidence of achlorhydria occurred amongst patients with anemia. This is quite in agreement with the findings of Rozendaal and Washburg (1938) who studied 906 cases from the files of the Mayo Clinic in which a definite diagnosis of pernicious anemia was made and found achlorhydria in all of them. Sturgis (1936) studied 600 cases of pernicious anemia and noticed the same thing in almost all the cases.

Nausea, vomiting, heart-burn, and poor appetite in patients with diabetes led H. Blotner (1940) to investigate the possibility of any unusual changes in the chemistry of the gastric juice of such patients. He found that in patients with diabetes, there was an increased volume of gastric juice, a higher degree of acidity and increased pepsin and rennin content. The injection of pituitrin inhibited these effects. Because of these findings it was suggested that the posterior lobe of pituitary gland had some control over the gastric secretion.

It is a matter of frequent observation that patients with duodenal ulcer secrete more gastric juice rich in hydrochloric acid than normal individuals having no complaints relating to gastro-intestinal tract. Winkelstein (1935) has shown that the gastric secretion of patients having duodenal ulcer is definitely higher in acid concentration and greater in volume than that of normal subjects. Stevens et al (1939) tried to suppress the gastric secretion by introducing 0.4 per cent hydrochloric acid solution into the duodenum of duodenal ulcer patients, but they noticed no constant and significant effect on gastric secretory curve. A. F. Hurst (1929) was impressed by the occurrence of duodenal ulcer in people who already had hyperacidity. No less than 90 per cent of 114 patients with duodenal ulcer had hyperacidity, and 10 per cent had normal acidity. Polland (1933) studied 133 cases of duodenal ulcer and found that 91.3 per cent of the patients had total acidity higher than the mean values of normal persons of the same age and sex. In cases of peptic ulcer it is the observation of most workers that there are no constant or significant findings after gastric analysis. Hurst observed in 53 cases of gastric ulcer, 58.4 per cent with hyperacidity and 32.1 per cent with normal acidity.

The diseases in which the gastric acidity falls below normal are mainly pernicious anemia and cancer of the stomach. In these diseases generally the gastric secretion is low and the acidity is below normal. They represent the cases of true achlorhydria as against pseudo-achlorhydria. These conditions can be differentiated by a study of gastric acidity after an injection of histamine. Ivy and his co-workers (1937) considered histamine as a gastric secretory hormone, having isolated and identified it chemically. Polland et al (1930) have shown that gastric curves after histamine injection have a diagnostic value in cases of cancer of the stomach.

The causes leading to anacidity in pernicious anemia and cancer of the stomach are not yet clearly understood. After analyzing the gastric contents of 79 patients, before and after treatment of cancer, Comfort, Butsch, and Eusterman su



not due to the effect of the malignant growth but probably a cause leading to such growth Hurst (1936) was of opinion that achlorhydria in cancer of the stomach was really due to chronic gastritis which was present before the growth developed J B Kirsner (1940) did not discover any correlation between the degree of acidity of gastric juice and the gastroscopic appearance of gastric mucosa of patients with pernicious anemia and cancer of the stomach

From the frequent observation, that anacidity in cancer and anemia is not necessarily due to a chronic inflammation of mucous membrane, led A Brunschwig et al (1939, 1941) to investigate the problem from another point of view They worked on the hypothesis that achlorhydria may be due to the presence of a gastric secretory depressant in the mucous lining of the stomach, which might have formed during the process of cancerisation They injected intravenously a tissue extract of cancerous stomachs into pouched dogs and observed its inhibitory action on their gastric secretion The achlorhydria produced was transitory Similar phenomenon was observed when gastric juices from patients with pernicious anemia and cancer of the stomach were injected intravenously into dogs Ivy (1937), was of opinion that the factor which inhibits gastric secretion may be a hormone 'enterogastrone' which is formed in the duodenum following an ingestion of fat Although all workers agree as to the presence of gastric depressant in the mucous lining of the stomach of the patients with pernicious anemia and cancer of the stomach, yet its nature and the mechanism by which it is formed are not known

As a study of gastric analysis appears to be a valuable diagnostic aid in diseases of the stomach The following data obtained at this hospital was scrutinised in the light of the above mentioned considerations

During the last three years gastric analysis was carried out as a routine measure in patients presenting clinical signs of disease of the stomach or duodenum The method employed was as follows The patient was asked to fast for 12 hours and only a light supper was allowed on the previous night In the morning, the stomach was emptied by passing Ryle's tube The test meal used was 50 cc of 7 per cent alcohol which was immediately administered through the same tube Seven different samples were drawn out at intervals of 15 minutes The cases have been classified as anacidity, lower acidity, normal acidity and hyperacidity, according to the standards laid down by L E Napier Results of such analyses are shown in the following table

TABLE

Disease	No of cases	Gastric Acidity			
		Anacidity	Lower	Normal	Hyper
Cancer of Stomach	24	12	9		3
Duodenal Ulcer	7			1	6
Gastric Ulcer	5		2	2	1

In all 36 cases were studied in this manner. There were 24 cases of carcinoma of stomach, of which 12 showed complete anacidity, nine showed reduced acidity and three showed hyperacidity. Seven cases were of duodenal ulcer, of which six showed hyperacidity and only one gave normal response. Five cases belong to a group of gastric ulcers, of which two showed reduced acidity, one hyperacidity and the remaining two gave a normal response.

These findings suggest that the study of gastric secretion is a useful procedure in cases of cancer of the stomach. It is also useful in duodenal ulcers, where the acidity is usually high. In cases of gastric ulcers, the study does not give equally useful information since there is usually a normal response. But these findings can be utilised to differentiate gastric ulcer from the other two conditions in conjunction with other clinical findings.

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## MENSTRUATION AND ITS IRREGULARITIES

### A STATISTICAL STUDY

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Menstruation and its irregularities form the basis of diagnosis in clinical gynaecology. A detailed study of the accurately kept data from gynaecological patients has recently cleared up the symptomatology of many of the gynaecological lesions and has helped a great

A paper read at the 45th Meeting of Seth G S Medical College and K E M Hospital Staff Society, Bombay on February 10 1945 with Dr K M Masani, M D in the chair

deal in coming to a definite diagnosis of the lesions which are characterised by absence of any palpable P V finding in the pelvis. Most of these lesions in the older days were treated by radical operation of extirpation of the uterus so as to stop permanently the menstrual function and bring to an end once for all the great inconvenience caused by the irregularly occurring menstruation. If the patient was too reluctant to undergo the major operation, the radiologist was ever willing to come to the rescue of this nervous patient with the help of his gigantic machine to destroy the functions of the ovaries and leave the patient with more nervous symptoms than before. The menstrual irregularities produced by the medical and surgical lesions outside the genital tract have also been studied in the recent years from various aspects. I could find very little publication in the Indian medical literature excepting a few papers. I had solely to rely on the histories from my private hospital patients which I have personally collected with good deal of details as I wanted to study in series the histopathological changes taking place in the endometrium throughout the menstrual cycle. The material was collected during my histopathological endometrial study, which I had the privilege to carry out under the able guidance of Dr V R Khanolkar in the research laboratories of the Tata Memorial Hospital during the last three years. These patients during the investigation were submitted to repeated curettage and suction biopsies of the endometrium whenever it was found possible and necessary during the different stages of the menstrual cycle and accurate information had to be gathered as regards the menstrual cycles. Naturally the material so collected is bound to be fairly accurate and can be relied upon to derive the averages. In addition to this, the data had to be gathered from the lay people, mainly friends and acquaintances who were sufficiently educated and who showed no objections whatsoever in revealing their menstrual history. For the purpose of working out the statistics and percentages, hundred subjects who considered themselves quite fit and not needing medical treatment were interviewed and the figures were used as control in the comparison with the data of the hospital patients.

TABLE I

Total number of private cases investigated for the statistic	1006
Normal educated women without gynaecc. complaint	100
Operated upon for	250
Major minor or	{ Cases of primary sterility Cases of Secondary sterility
radium operation	
	{ Pts. with functional inflammatory, and neoplastic diseases
	560

TABLE II

Particulars of investigations of 100 normal women (educated)

(a) Age Distribution		(b) Geographical Distribution	
Age Group	No. of cases	Place	No. of cases.
20—24	45	Bombay	63
25—29	32	Gujerath	20
30—35	15	Karwar	18
36—39	8	Belgaum	2
		C P	2

(c) Communal Distribution.		(d) Marital Distribution		(e) Previous Menstrual Cycle	
Community	No. of cases		No. of cases		No. of cases.
Hindu	95	Unmarried	73	Regular	41
Parsi	2	Married Nullipara	10	Irregular	50
Christian	3	Married Multipara	17		
				Total	100
	Total 100		Total 100		

Thus it will be seen that the majority of the normal women were in the child-bearing age and more than 80 per cent of them were either unmarried or nulliparas i.e. their sexual cycles were not disturbed by the occurrence of previous pregnancy. Practically 95 per cent of women were Hindus and were not having pure non-vegetarian diet but mainly vegetarian or mixed type. It will be seen that even though the women were considering themselves quite healthy and normal, about 51 per cent of them gave the history that the past menstrual periods were irregular and only 39 were quite confident about the regularity of the previous menstrual cycles. But even among these persons I am sure, if one was to obtain the history by regularly keeping the calendar record of their menstrual returns, some of them would have dropped out from the normal group. It is a curious fact to note that on studying the present menstrual cycles of these 100 persons, the same figure was obtained for normal cycle (39 per cent in table III).

In order to study the wide variation noted in the duration of the interval and duration of blood loss, the normal and diseased cases were studied from this point of view. But before I refer to these tables I hope I will be excused for explaining the terminology that has been used throughout this investigation, since it differs a little from the other investigations. Moreover, one finds in the literature a wide divergence as regards this terminology both in the British and in the Continental or American workers. In the presence of such a chaos I think it would be worthwhile to express the significance of their words with which they are used. The normal cycle is taken as one in which the woman menstruates for 3—5 days with normal flow and at the interval of 26—32 days. Oligomenorrhoea means a similar cycle with scanty blood loss in duration and flow. Polymenorrhoea indicates the cycle at shorter interval of 15—25 days but the blood loss is scanty while polymenorrhagic means the shorter interval with profuse and prolonged loss. The hypomenorrhoea and hypomenorrhagia are applied with the same significance, only the interval of the cycle is from 5—12 weeks or so. Menorrhagia and metrorrhagia are the terms which are used with the usual conventional meanings, the former indicating the excessive loss with normal interval and the latter, the inter-menstrual bleeding. I have purposely collected the continuous bleeding group as a separate one and I feel that this group should be sub-divided into nine sub-groups as I will explain later on, when I deal with that abnormality, and at the same time the most important group in details.

TABLE  
Incidence of various menstrual cycles  
Normal cases compared with sterility group and diseased group.

Type of Cycle	Normal group 100 cases	Primary Sterility 250 cases	Secondary Sterility 80 cases	Combined 340 cases	Diseased group 568 cases
Post menopausal Amenorrhoea	Nil	Nil	Nil	Nil	2.05%
Amenorrhoea	Nil	Nil	Nil	Nil	2.13%
Hypomenorrhoea	5%	14%	5.55%	11.75	1.6%
Polymenorrhoea	1	10.4	8.88	9.99	2.82%
Oligomenorrhoea	29	22.4	27.75	23.81	8.65%
Normal	39	18	22.2	19.11	15.2%
Menorrhagia	21	13.6	11.1	12.93	16.78%
Polymenorrhagia	4	12	21.09	14.4	15.9%
Hypomenorrhagia	1	7.6	2.22	6.17	6.9%
Continuous bleeding	Nil	2.0	1.11	1.76	27.38%

The table III is prepared with the idea of studying the per centage incidence of each type of menstrual cycle in the normal, sterility group and the diseased group

In short the sterility group as a whole has more tendency to show some type of menstrual abnormality. The normal cycle is less frequently present than in the control group. They frequently show scanty menstrual loss with short or long intervals (poly and hypomenorrhoea) as in primary sterility group and periods at shorter intervals with profuse loss especially in the secondary sterility group. The clinical interpretation that may be summarised from these data are that in these patients who suffer from sterility which is caused not by the infective, neoplastic or displacement factors but by purely functional origin either in the ovaries or endometrium, the normal menstrual cycle is upset. This may be attributed to irregular ovulation taking place in the ovary. Since these patients get the uterine bleedings in some cases scanty and in other even profuse either at shorter interval of 15—21 days or longer intervals of 1½ to 3 months or so, they are rendered sterile by the improper functioning of the ovaries. Those who have secondary sterility may be supposed to have ovulatory cycles and actual menstruation and among them polymenorrhoea and polymenorrhagia seems to be common. Ovulation, though it may be taking place, cannot prolong the cycle to the normal length of 28—30 days' interval. No doubt the mechanical factor of the blockage of the tube is also existing in these patients. The primary sterility group, showing uterine bleeding of the nature of polymenorrhoea, polymenorrhagia, hypomenorrhoea, hypomenorrhagia and with comparatively less frequent normal rhythm suffer from primary or initial lack of ovulation and the effects of this on the endometrial picture will have to be kept in mind during the histological study.

The next problem investigated was the age of menarche or the onset of menstruation among the Indian women of our part of the country, and if it has any relation to subsequent development of sterility and other organic and functional diseases in the genital tract. According to Curjel's investigation of Indians, the childhood marriages with its consequent early stimulation of the genital organs did not

lead to early appearance of menses. Fluhmann has found that the age of onset in the vast majority of American girls varies from eleven to sixteen years, the mean generally has been found somewhere between 13 and 14. These figures are decidedly lower than many of the western European nations. Russia and Scotland 15.03, 15.2 Germany and Poland 15. The figures for Asiatics are definitely lower. Those for Japan and China are round about 14 and for north Indian women as reported by Curjel they are 13.63. I have found the figures practically similar—the actual figures for my normal group is 13.6 and for the hospital patients 14.05.

On detailed study of the sub-group certain following facts are vividly brought out namely

1. No material differences are noted in the average figures of different group of hospital patients.

2. Excessive loss and particularly shorter menstrual intervals are seen in women who have early onset of menstruation. Scanty loss and longer intervals are seen among those who start their menstrual life rather late.

3. "The age of onset of menstruation varies directly with the interval of the cycle" is well brought out by the table of the diseased group. Patients with polymenorrhoea and polymenorrhagia, which are supposed to have defective corpus luteum formation in spite of ovulation are seen to have earlier menarche than in those with normal cycle. The patients with hypomenorrhoea and hypomenorrhagia and amenorrhoea with defective ovulation have late onset of menarche.

Thus the age at menarche is a fairly accurate barometer of the mental and physical development of the puberal girl though menarche is only one of the many manifestations of puberty and may appear any time during this phase of life. There is a world-wide decrease in the age of menarche probably because of the altered standard of hygiene and diet, but according to the above conclusions it may render the race more susceptible to menstrual irregularity of the nature of polymenorrhoea, polymenorrhagia and continuous bleeding of functional origin.

TABLE IV  
MENSTRUAL CYCLES IN 566 DISEASED CASES

Type of Cycle		No. of Cases	Percentage
Post Menopausal Amenorrhoea		15	2.66
Amenorrhoea (Child bearing period)		12	2.12
Hypomenorrhoea		9	1.6
Polymenorrhoea		16	2.82
Oligomenorrhoea		49	8.65
Normal Cycle		86	15.2
Menorrhagia		95	16.78
Polymenorrhagia	A 50 } B 40 }	90	15.90
Hypomenorrhagia		30	5.3
Continuous Bleeding		155	27.38
Total		566	100

Table 4 gives in short the type of menstrual irregularity in 566 diseased cases and also the percentage incidence of each group.

## THE CONTINUOUS BLEEDING GROUP

This seems to me the most important group in the whole series and it should receive attention from quite a different view point than is being considered at the present day. Cases should be always sub-grouped into eight varieties and not all collected together into common group. This will facilitate coming to a more exactness in the clinical diagnosis and will also help in the study of the endometrical picture so as to come to the root cause. There were 155 cases of this group i.e., about 27 per cent of the whole diseased group and really 40 per cent of the bleeding group. I have grouped these cases into following sub-groups —

		Percentage
1	Post Menopausal continuous bleeding 5 cases	3.23
2	Continuous bleeding preceded by Amenorrhoea cycle 7	4.51
3	" " following one period of Amenorrhoea 10 cases	12.25
4	" " following full time labour or abortion (no amenorrhoea after abortion or labour) 21 cases	13.55
5	" " during lactation Amenorrhoea 2 cases	1.25
6	" " following a normal period 18 cases	11.61
7	" " following previous Menorrhagia 34 cases	21.93
8	Irregular bleeding or Metrorrhagia 40 cases	31.6

The significance of this sub-division will be well-appreciated by those to whose lot falls the most annoying problem of diagnosing the condition especially when, along with the complicated menstrual bleeding, the P V findings of the cases are not far from the normal. Hence, before I could draw some conclusion from the endometrial study of this group I thought it worthwhile noting clinically what organic functional lesions are likely to exist in the pelvis to give rise to each type of menstrual abnormality.

## POST MENOPAUSAL CONTINUOUS BLEEDING

There were five cases of this group. Two were lesions of the cervix, one a *benign polyp* and another *endocervical carcinoma*. In the remaining three cases, ovary was responsible for the uterine bleeding. The lesions noted in the ovary were *granulosa cell tumour*, *theca cell tumour* and *endometrioma of the ovary* (post radiation bleeding). Excepting the first two lesions in the cervix the rest of these can easily be missed in early stages and the real cause can only be detected when the operative removal of genital organs as restored to or the tumour grows in size sufficiently to be detected by palpitation. These cases may often be mistaken for cancer of the body of the uterus if no endometrial study is undertaken and ineffective and improper line of treatment may be undertaken. The theca cell tumour in my series was suspected only after the study of the endometrium and the uterus and the small tumour of the ovary were taken out by subsequent vaginal hysterectomy.

## CONTINUOUS BLEEDING PRECEDED BY AMENORRHOE CYCLE

Majority of the cases belonging to this group are of the nature of *metropathia*. But one important point that is brought out is the fact that a serious mistake may be made in missing an *earlier ectopic pregnancy* existing in this type of menstrual disorder.

## CONTINUOUS BLEEDING FOLLOWING ONE PERIOD OF AMENORRHOEA

There is an usual tendency to regard cases of continuous bleeding following a period of amenorrhoea as cases of *abortions* and *ectopic pregnancy*. But the possibility of the *metropathia* and even *persisting corpus luteal cyst* with pseudopregnancy must also be kept in mind. In one of my cases of this group there was a small ovarian abscess in the pelvis which had given rise to continuous bleeding preceded by a period of amenorrhoea. Such case may be mistaken for ectopic pregnancy as was done in my cases. A corpus luteal cyst and an ovarian dermoid may give to a similar clinical friction and to complicate the matter still further. The A Z Test may even prove mildly, positive in these cases.

CONTINUOUS BLEEDING FOLLOWING FULL TIME LABOUR OR ABORTION  
(no amenorrhoea after labour or abortion)

There were 21 cases, naturally *incomplete abortions*, *bloodmole*, *placental polyp* and *acute sub-involution* from the major part of the list. This group is bound to be bigger still had I taken all the abortion cases into consideration. But only those cases are included which were doubtful as regards the diagnosis and the latter was confirmed only by microscopic examination. But a special reference must be made to *inversion of the uterus* and *twisting of an ovarian cyst* and particularly a uterine fibroid, which became sub-mucous and pedunculated during the puerperium and gave rise to obstructive symptoms in the pelvis with profuse bleeding.

## CONTINUOUS BLEEDING FOLLOWING LACTATION AMENORRHOEA

There were only two cases and both the cases were of pregnancy taking place in the tube and ending in acute abdomen requiring operation. Just as intrauterine pregnancy or acute infection during lactation amenorrhoea is always first excluded one should always have the *ectopic pregnancy* also in mind.

## METRORRHAGIA OR IRREGULAR BLEEDING

This is the most common group. It is a menstrual irregularity often associated with definite organic lesion which can be easily detected by careful and thorough examination. Cancer of the cervix forms the major portion and as the physician easily detects it, I need not deal with it at length. But before I consider the next group I will like to bring to the notice the two cases of ectopic pregnancy in the list, which may be completely overlooked.

## CONTINUOUS BLEEDING FOLLOWING MENORRHAGIA OR POLYMENORRHAGIA

There were 34 cases. All the organic and the functional lesions which are associated with menorrhagia and polymenorrhoea have a tendency in the latter stages to show a tendency towards continuous bleeding. It is a well-known fact that interstitial fibroids with menorrhagia begin to bleed continuously as soon as the growth ulcerates after it has become sub-mucous and pedunculated. A similar change in the symptoms is seen in the cases of *metropathia* and *chronic sub-involution* and *metritis*, and it will really be worthwhile noting the



changes produced in the endometrium during such a bout of haemorrhage, and if such a change does exist what relation has it got to the malignant transformation of an overactive and oversensitive endometrium

#### CONTINUOUS BLEEDING FOLLOWING A NORMAL PERIOD

This seems to be the most interesting type of bleeding, which may try the skill of a gynaecologist in his diagnosis. An organic lesion, if present in such cases has not advanced sufficiently to give definite information by P V examination alone. Exception must be made of the acute painful lesions e.g. *extra uterine pregnancy*, *twisted ovarian cyst*, *salpingo-oophoritis* and *ovarian abscess*, when the P V findings do not show any appreciable enlargement of the uterus the diagnosis of *metropathia*, *early abortions* and *Pankow's disease* can only be confirmed by microscopic examination of the endometrium.

Having discussed the various types of menstrual irregularities, it becomes evident that in the present advanced knowledge of menstrual disorders, obtained by detailed study of menstrual histories, it is high time that the symptomatology of many of the gynaecological diseases needs thorough reconsideration particularly from the viewpoint of uterine bleeding. I have carried out the investigations on that line but it will be really suitable to consider the problem along with the study of the endometrium in a subsequent paper. Such a study will certainly check the present tendency of practicing gynaecologist to diagnose each and every lesion with abnormal menstruation as functional in origin and treat such abnormal manifestations blindly without proper investigation by a series of recently available hormone preparations.

I do not intend to deal with the treatment of all the varieties of uterine bleeding. But I must not fail to mention some of the recent changing concept of metabolism of oestrin in the human body. The work of Biskinds has shown that rat's liver loses its ability to inactivate oestrogen in the deficiency of vitamin B complex. The ability to inactivate androgens however was not lost.

One can thus surmise that in the presence of deficiency of vitamin B complex the oestrin may not be fully metabolised or may be metabolised in the wrong direction which may give rise to the upsetting of the normal function of the pituitary and also functional uterine bleeding from the endometrium. I have tried this line of treatment with massive doses of vitamin B complex injections, (Lederle) as well as by mouth in form of beplex tablet without an associated hormone therapy and the results are seen to be quite encouraging, in checking bleeding and in regulating subsequent menstrual cycles. The number of patients so far treated is small for statistical evaluation yet a mention is made here with the idea that a similar series of patients suffering from functional uterine bleeding may be studied by the other members of the staff and a fair bulk of material will then be available to substantiate clinically the laboratory investigations in view at present.

# DISCUSSION



**Dr Z J Joseph** said "In no other field of gynaecology is x-ray radiation more helpful and useful than in the treatment of functional disturbances of the ovaries and sterility. There is considerable prejudice in the profession against irradiation for therapeutic purposes as it is thought that it might harm the mother and the foetus. Irradiation during pregnancy is in many instances harmful to the unborn, the harm depending on the age of the embryo and the amount of radiation given.

Small doses of deep x-rays are given to the ovaries and the pituitary gland. The mode of action of the x-ray is not yet clearly understood. Recent studies in hormone secretions have shown undoubted relationship between the ovaries and the pituitary gland. The normal genital function of the female depends upon proper correlation between the ovary, pituitary and the uterus.

Contraindications are pelvic inflammations and early pregnancy. Sexual relations should be forbidden during the course of radiation therapy.

The technique followed in this hospital is as follows:

High voltage therapy is given in all the cases. The pituitary gland, and the ovaries are exposed to deep x-rays once a week. 80 'r' units measured in air at 150 K V are delivered to the pituitary and to the ovaries once a week, the field for the pituitary being  $6 \times 8$  cms and for both the ovaries  $20 \times 24$  cms. The treatment lasts 3 weeks.

Kaplan (A J Roentgenology November 1939) treated in a similar way 194 cases. Of these he was able to follow up 156 cases, the menses were regulated in 103 cases and there was no improvement in the remaining 53 cases. The oldest patient was of 45 years and the youngest of 19 years. Of these 103 patients in whom menstruation was re-established, 51 became pregnant. A similar line of treatment is being followed in this hospital in such cases and when sufficient data is available, the results will be presented."

**Dr V R Khanolkar** said that the investigations carried out by **Dr B N Purandare** had several interesting features which needed emphasising. The work was started nearly  $2\frac{1}{2}$  years ago for a study of endometrial biopsies from patients who presented themselves with irregularities of menstruation. On analysing our material it was soon evident that such material would not yield much useful information unless it was accompanied by a careful clinical study of those cases. **Dr B N Purandare** therefore restricted himself to cases which had been clinically studied by him personally and the present paper was an outcome of this preliminary clinical study. It had already yielded fruitful data far beyond our expectation, and has demonstrated that some of the generally accepted ideas on the subject may need revision in light of the new facts which had been discovered. He further suggested that **Dr Joseph** should avail himself of the clinical and laboratory facilities available at the K E M Hospital before assessing the value of x-ray treatment in the cases which he had referred to.

Dr J N Karande said that co-operation between the gynaecologist and pathologist was essential in the evaluation of these cases

Dr B N Purandare said that as regards the normal cycle at regular shorter rhythm one should not consider them normal, only because they appeared at the same interval. The polymenorrhoeic type of cycles always indicated defective corpus luteal phase and investigations on the patients should be carried out on those lines. He then congratulated Dr Joseph for the good results he obtained by giving stimulating doses of x-ray to the pituitary and ovaries in cases of functional uterine bleeding. He however, suggested that such treatment should be undertaken with greatest care especially in young girls. He then cited a case who after receiving x-ray treatment, got married and was investigated for not conceiving even though she was having regular periods at the interval of 45 days. The repeated suction biopsies at the proper time of the menstrual cycle failed to show any evidence of the secretory change in the endometrium.

## SCIENCE AND THE STUDENT

V R KHANOLKAR,

Director of Laboratories, Tata Memorial Hospital, Bombay

When I was asked to address you this evening, I agreed to do so with some hesitation. It is several years now, since I was associated with the doubts of youthful minds. The conditions are changing so rapidly all over the world, that I feel, as if I had lost touch with the new generation, its aspirations and its foibles. But some points of contact still remain. You have embarked on a career of scientific study, I did so thirty years ago, and still feel like a beginner. When I joined a college in my city, it was considered the correct thing to go in for an arts course and then branch off to one of the so-called noble professions. Our highest ambition was to be admitted one day in one of the Imperial Services or end up as a judge in a High Court. As students we had lengthy discussions, as to the type of study which was more elevating to the mind, and we had most of us decided that a study of literature, history and law was more ennobling than any other human pursuit. A few cranks amongst us selected science, but were usually looked down upon, by the majority of our fellow students.

As I said before conditions have changed greatly in the last thirty years and the evidence is not far to seek. Every college in our cities has a large list of students who desire admission to a science course, and many are turned away for lack of sufficient facilities. What has brought about this change? Have we as a country become more science-minded or is it that a science course holds promise of better prospects in later life to our young men? I wonder what your answer would be, to this question. Have you any idea as to what a study of the natural sciences is going to offer you in the way of intellectual

satisfaction? It is likely that you have not worried over this question or that some have never felt the need for doing so. And yet it is a question which you have to put clearly before yourself, if you wish to take an active part in the reawakening of our country. If the young men remain interested only in jobs and not in science, if they are not concerned with the new outlook on life that it opens up to them, we shall continue to be a nation of small job holders and imitators relying for all advance and inspiration on foreign countries. There is however a ray of hope. Asiatic people have learnt a few important lessons in the period between the two world wars. For instance we have recognised the necessity of industrialisation and technological advancement if we wish to attain our rightful place in the community of nations. It is true that we are suffering from our growing pains and are buffeted with conflicting ideas and emotions. However that may be, we cannot afford to hide our heads from realities. If we must live and survive, we have got to proceed along the path of the fullest development of our own resources, and what is more important we have got to keep on progressing. If we falter or slacken speed, we shall have to pay the penalty for our indolence, as our predecessors have paid and as we continue to do even today. We have therefore to ask ourselves, how could we achieve eminence in science as our ancestors did in art and philosophy. How could we regain our place among the leaders of thought in a rapidly changing world. I believe that this could be achieved only, when we begin to live and have our being in an atmosphere of scientific thinking, instead of just passing degrees and diplomas in a science course.

You would naturally like to know what is this scientific thinking, and how it differs from any other kind of thought. Man, from the earliest glimmerings of his history has been bewildered and perplexed by the natural events occurring round him. He found that he had no control over these happenings. He was frightened by lightening and thunder. He suffered from floods and droughts. He marvelled at light and darkness, at the changing of seasons, at the sprouting of leaves at the song of the birds and at the birth of his own kind. He has been scared by disease and by death. And he has tried to explain all these things to himself, to get some peace of mind, some respite from a feeling of helplessness and utter impuissance. There are two ways in which he has tried to understand and explain natural phenomena and to make his world safe for himself.

The first and the oldest way is one, in which gifted men have thought and pondered over the mysteries of life and death, man and the universe and their relation one to the other. They have woven fantastic webs of fancy which have given them and their followers faith and hope and probably happiness. Every country, every society however primitive had its prophets and its seers, who have contemplated long and deep, have uttered words of ecstasy and rapture, under starlit skies, on desert sands, in caves and on the hill tops, under trees besides mighty rivers and in dark and fearsome forests. Our ancestors

have burst out in wonderful song and beautiful lyrics when possessed of these inspired ideas. Their ideas have permeated the whole fabric of our society, the very essence of our being, for centuries past. The essential content of all these ideas, the central thread which has held them together was a dogma which had to be accepted "as a complete belief, forthright and unquestioning." You had to believe the whole "creed" in its minutest details and if you desired peace—here and hereafter—you had to stifle any questionings or doubts that may arise in your mind. All utterances were final, needed no alteration in the light of newer facts, because they were not based on fact. In many cases the outpourings of fevered minds appear to us ridiculous to-day, but were the basis of learned discourses and even disputes a few hundred years ago. For instance they described the minute anatomy of hypothetical animals, like the dragon and the unicorn, without ever having seen a single specimen, or the dresses of the fairies and the pranks of the demons with relish and with gusto. Now you could see for yourself how such thinking was self limited, by its very nature. You could add flourishes to it, rebel against it, replace it by a new dogma, but you could never progress with it. And that is what we have done and are still doing.

The other way of thinking is of recent growth, only a few hundred years old. It began in a small way, hesitantly, with many misgivings and much doubt. With the advent of years it has grown in power and scope and has now begun to invade the most sacred realms of thought: the behaviour of man, his social habits, and his political beliefs. This is the scientific way of thinking. How does it differ from dogma? It is an organised attempt not of an individual, but of mankind to discover how things work in relation to one another. Its findings are not final and unconditional and in no case such, that evidence becomes irrelevant. It is based on probabilities, rather than certainties. It has thus in its very nature the possibilities of improvement and progress, with the access of fresher knowledge and more accurate facts. It has brought us enormous power and there is no limit to where it may lead us in future. It is not the achievement of a few isolated men of genius. The enormous advances in knowledge and understanding even in the last few years are the outcome of the efforts of a large number of people, some brilliant, some good, others not so good, but all working on a solid stratum of facts and more facts. Let me give you a few examples to illustrate what I have been saying. When Newton about 250 years ago placed a prism of glass in the path of a beam of light he saw that the emerging beam was split into seven colours. He did not burst into song about the beauty of the seven colours, nor did he fashion a toy out of it to amuse his people. He began to study the cause of the production of spectrum. This study has led to a profound understanding of the nature of light rays, not only visible but also invisible. Who could have imagined a couple of centuries ago that this simple observation would lead to methods of spectrophotometric analysis of minute quantities of matter or a study of electrones,

or who could have guessed that this knowledge would be used in the detection of substances which produce cancer in man? And yet these are the actual problems in many physics laboratories. Our ancestors had seen the rainbow and written about its beauties, but it remained for laboratory workers to investigate its nature and to apply the knowledge which was acquired for practical ends. And so knowledge marches on, heaping fact on fact, till its limits are lost in speculation. Take another example. Hardly a hundred years ago a young French chemist was led to a study of fermentation in vinegar, and the disease pebrine in silk worms. Both vinegar and silk were articles of great economic value to his country and both were subject to sudden deterioration for some unknown reason. Philosophers and wise men had talked for centuries about natural deterioration and about spontaneous generation of living beings, and nobody could dare to dispute their assertions. Louis Pasteur set out to study these problems and within a few years had discovered the cause of these calamities, had proved that there was no spontaneous generation of organised living beings and had incidentally laid the foundations of a new science, microbiology. The newer knowledge has revolutionised our ideas about disease. It has made possible intravenous therapy and modern surgery. It has also supplied a rational basis to the many administrative enactments, which are designed to control or arrest epidemic diseases. We are now probing the realms of micro-organisms invisible even to high power microscopes and are enlarging our frontiers to a border-zone between living beings and inanimate objects, the bacteriophages, the viruses and the enzymes. Just one more example, and one could cite hundred others to emphasise the same features. An Austrian monk Gregor Mendel started to study the transmission of characters in flowering peas in a monastery in Czechoslovakia about 75 years ago. Up to that time all sorts of quaint ideas were current regarding heredity. The patient work of a monk unknown and unrecognised by most of his contemporaries has laid the foundations of the new science of genetics, which has sent its ramifications in agriculture, animal husbandry, medicine and sociology. We thus see that scientific thought has steadily built up a body of fact and theory which has pervaded all countries and has supplied basic principles with common past and let us hope a common future. It started as a hobby for men with sufficient means, with avowedly unorthodox tastes and possibly unacceptable ideas. Towards the second half of the last century, science came into its own and conquered the opposition of society. And now, we are finding that in peace as in war (unfortunately more in war) the essential machines of industry and modern warfare can be run by comparatively few people with sufficient scientific training. One of the allied leaders is said to have made a statement that "A hundred physicists in this war are worth a million soldiers". But even though science is receiving an increasing recognition in many countries, much confusion prevails in the minds of most people regarding its content, its aims and its objectives. They are not yet quite sure whether it is not

"just a collection of tricks which happen to come off", or whether it is not a means for increasing the creature comforts of civilised nations. It is not necessary to go into many of these misconceptions. I will deal with only two of them.

Whenever one talks of science an average person thinks of the electric light, the railway train, the radio, the aeroplane and so on. These are the applications of scientific ideas to technical problems. They are the bye-products of scientific thinking. The new gadgets, or improved standards of living, or even better health and longer life, are the obvious and direct results of applied science. The person who is a technical expert need not necessarily be a man who thinks scientifically.

The emphasis in our science institutions and colleges has been to make people technical experts and not scientific thinkers. You cram formulae and equations and pass examinations, in say, physics or physiology. You hold important appointments and direct industries, but your thinking may still remain unscientific and confused. If I had my way, I would rather initiate you into scientific method and create a scientific attitude in your minds, so that you could later apply it to social, political or technical problems. No real scientific progress will be possible in our country, unless our young men are disciplined to think scientifically.

Another confusion arises from the fact that you will be told that science has made men materialistic, that it has led to enormous destructive tendencies in people, that it has brought war and strife and hatred in the world, and has taken away the joy of work from industry, and joy of living from all. Knowing that all these happenings are present in the world today can the blame be placed on science or the scientific way of thinking for the present state of affairs? It is true, that the countries which have shown marked advance in scientific development have also let loose the most destructive wars on earth. Their growing industries have been followed by relentless exploitation of technically backward countries. But all this has been brought about not because such things are inherent in scientific progress, but because the immense power which has been made available by science is still being wielded by men who think and feel and act, as their ancestors did centuries ago. It is necessary to get a correct perspective in time, to appreciate why men are behaving as they are to-day. Supposing we compressed the achievements of the whole human race on earth, to the life time of one generation of people say 50 years old. In such a case the time scale would be roughly reduced by ten thousand and each year in the life of the generation would correspond to ten thousand years in the progress of the human race. Now let us visualise the main stages in the progress on this time scale. It would appear then that until last year when the people of this generation were 49 years old, they were roaming for food, living in caves and wandering after herds of animals, in the hope of killing a straggler. About twelve months ago they had begun to settle down in places, harvest-

ing for food, domesticating animals and weaving coarse garments Six months later they had invented writing and one group had already advanced far in literature, art and philosophy Only a couple of months ago Jesus, Sidhartha, and Lao Tse had preached their wonderful teachings According to this time scale the printing press would be a fortnight old and the steam engine a discovery of last week How could one expect then, that men who have lived, as cruel, rough, untamed savages until last year would behave otherwise than by using the great discoveries and enormous power which science had placed in their hands a couple of hours ago, except in the prosecution of a ruthless devastating war

Another approach to an understanding of the reason for this peculiar behaviour of human beings is furnished by the work of psychologists during the last 40 years This work may be said to have started with Alfred Binet the French psychologist and carried on with brilliance by Spearman, Kohler and Terman Let me tell you some of the revolutionary findings of their careful work They found as a result of accurate tests on thousands of children and adults that —

1 Our abilities are constructed of a single large general ability, working in association with a large number of special abilities We may designate this capacity as intelligence, which is the ability to think abstractly, or an adaptability to new situations

2 The normal growth of intelligence is most rapid in the early years It is greater between 3 and 7 than between 8 and 13 years Between 13 and 14 it is very slight, and after 14 it is negligible Knowledge, wisdom, tact and skill come from experience, but the development of mind reaches its zenith between 13 and 14 years

3 In spite of differing home and school environments, the intelligence quotient of each child tends to remain a constant and that the sudden ups and downs in individual performances are not due to real changes in intelligence but to changes in interest, temperament, health and opportunity

4 Intelligence in any homogenous population is distributed with symmetrical frequency

This knowledge should supply a basis for the methods of our education There is at present a great upsurge in many departments of human endeavour Conferences and committees are meeting, to devise plans for the fashioning of a brave new post-war world which it is hoped would not plunge straight away into the follies of the old These are matters which deserve the attention of us all, because the future well-being of our children and their children depends on the outlook that is brought to bear on solving the problems of peace which will follow this war I should like to direct your attention to one small field of human activity, the medical education In most countries there has been a growing demand that something should be done to improve the character and alter the content of the education imparted to the undergraduates and post-graduates in medicine Many people who have pretensions to some experience in educational matters, and



others who have none, are clamouring for an urgent change in our curriculum, our methods of teaching and our teachers. All are agreed that the existing system is faulty, but none are in accord with the remedies suggested by others. Nowhere is this divergence of opinion more marked than in the organisation of post-graduate teaching in this or other countries. I believe that those who propose to effect improvements in the existing order of things should first obtain a correct measure of the problem before them. It is necessary that they should get a clear view of events which have culminated in the educational methods now in vogue. I would therefore present a brief glimpse of these events.

The beginnings of medicine are lost in a dim and distant past, and are probably coeval with the appearance of man in the dense forests of the quaternary period. Man, the hunter, must have watched his fellow man wounded and sore-stricken by his enemies. When living in communities he must have been baffled by the sudden onset of some diseases and their equally abrupt disappearance. It is therefore not surprising that the healing craft has, and continues to have its oldest associations with the priestcraft. A mystery and a dogma lies at the root of these two noble professions, and even though the labels have changed, they continue to do so to-day. In Babylon, ancient Egypt and India the priest and doctor were united in one person. We find however, from Eber's Papyrus that the physician, priest and magician had separated out in Egypt already in the 16th century before Christ. In Greece, the physicians were artisans, who wandered from place to place, and house to house, and offered their services like people of other crafts. They had their shops, their *tatretou* in which they looked after the sick and operated on patients, as you still see in some parts of India. In Rome, the doctors were slaves to begin with, and were valued almost as much as the eunuchs. In middle ages the physicians began to organise themselves in societies. Colleges of Physicians and Surgeons with their pompous regulations and elaborate ceremonial remind us of the guilds and vends in mediæval times.

The prestige of those who practised the healing art has varied from one era to another and one country to the next. All along its development however, it had its foundations in a craft. Medicine with its ancillary subjects is primarily a craft. A craft, can only be learnt by laborious apprenticeship, and those who wish to specialise in any of its branches must resign themselves to a lengthy vocational training with its emphasis on detail and familiarity with the unusual. No amount of book lore or learned disquisitions could make a man a master weaver or a competent goldsmith, a pathologist or a pediatrician. You have watched the sensitive hands of the potter at his wheel, coaxing the desired shape out of his clay or the deft fingers of a surgeon, sensing out the secrets from the hidden depths of his patient. Behind the deliberate, methodical, unhurried approach of an expert lie years of steady, intelligent study, laborious training and continuous practice. There are no short cuts and labour saving

devices for attaining excellence in any branch of medicine and the people who promise you rapid passage through the maze of techniques are ignorant of the complexities of their own subject. A good teacher may save the student from much that is insecure, uncertain and redundant, but now as ever before, medicine has to be learnt, it can rarely be taught. There is a popular belief that an untutored mind observes things as they are, whereas a trained person tries to see things which he is expected to see. Nothing could be more fallacious, as an untrained mind is shrouded in a fog, and accuracy in observation and precision in recording has to be acquired in the same slow way as a child has to learn to walk or to write.

The rapid progress of natural sciences during the last two centuries has had its repercussions on the healing art. Slowly, it began to divest itself of its many dogmatic wrappings and mystic lore, and clothe itself in a thin scientific veil. Now we have begun to speak of the art and the science of medicine. It has however to be confessed that the scientific development of medicine and its branches has been uneven and unequal.

All scientific study of any subject passes through four stages. At first there is a collection of observed phenomena and their detailed recording. This may be called the *descriptive stage*. The second is a *mensurative stage* when measurement replaces a qualitative description. In the third stage the mass of information is sorted, classified and the relevant separated from the spurious. This may be termed the *analytical stage*. In the final phase the whole of the available data are integrated into a hypothesis and information is transformed into knowledge, thus opening up fresh avenues for further advance in the subject.

It would be evident that most medical subjects have hardly evolved out of the descriptive stage, some have taken to measuring their findings and few to analysing the accumulated data. It is because of this unequal development that our ideas and methods of education in medicine are in their present chaotic stage, the requirements of physiology for instance which is becoming an exact science are opposed to that, let us say of dermatology which is still struggling to amass random observations. It may not be presumptuous therefore to state that under the existing conditions no homogeneity in training can be achieved and we could at best struggle to adapt our teaching to a maximum elimination of waste of the time of the student and labour of the teacher.

I would therefore suggest that medical education should aim at a threefold objective. The undergraduate training should be mainly concerned with broad principles and essential techniques. "The curriculum should be designed to give the student of average ability such knowledge and such education as will enable him to approach the problems of practice with some degree of confidence." It should be limited to that which is common, unequivocal and trustworthy. It should also provide opportunities and create a favourable

atmosphere for exceptional students to be initiated into advanced studies in subjects of their choice. The post-graduate training should be mainly devoted to a cultivation of technical skill in the different specialities. And, running throughout the undergraduate and post-graduate study, there should be a broad vein of theoretical training designed to develop a critical faculty and broad understanding of biological processes, in other words scientific thinking. "There can be few if any branches of science which have not contributed to the advancement of medical knowledge. There can be few, if any, branches of knowledge which have not been advanced by the labours of medical men." It is essential therefore that all schemes for advancement of medical knowledge should promote frequent contacts with workers in other sciences and encourage a "full scientific discipline and collaboration." All this would entail a marshalling of all our resources and a constructive co-ordination of the abilities of our teachers. It will also mean a new orientation in our acceptance of examinations as an evidence of training or aptitude in a subject. It is unfortunate that so far, the examinations have controlled what is learned by the students and therefore what is taught to them. This I submit is a wrong approach to education. These labels make the work of administrators and selecting authorities easy but exert a deadening influence on initiative and originality. You are all acquainted with the elaborate system of examinations for the selection of mandarins in the old Chinese bureaucratic hierarchy and the fossilising effect it has had on a highly cultured and intelligent people. It is time we emerged from the paralysing influence of the alphabetical adornments and initiated our young men into the realms of advanced and original studies. I must here utter a word of warning. We the old teachers have a peculiar conceit. We think that we can effect great changes by passing regulations and interfering with the time table of our students. Nothing could be more illusory, as many of us have found out after much bitter experience. What is needed is depth of knowledge and breadth of vision in our teachers and a keenness to learn in the taught, the rest will follow as a natural sequence of events.

I hope I have said enough to create in you an interest in the scientific method of thinking. It is necessary that you should begin to prepare yourself for tackling the big problems which you will soon be facing in a post-war world. There is a common excuse in most of our institutions that people do not get time to do original thinking because they are burdened with too much routine. I think you would be well advised to reflect on a few sentences that were recently written about a distinguished member of our profession, George Crile. "He never ignored an opportunity to learn from evidence at hand. Always he was observing, recording, correlating, devising theories and planning experiments to test them. No observation was too insignificant to engage his attention if it offered some clue to the answers he was seeking. In conversation and discussions with his colleagues he was alert to grasp any chance remark that may have a bearing on the

problem he was studying. Thus his work never degenerated into routine for he was always the investigator."

May I offer a word of advice before I finish. The study of science is an exacting process. You cannot gain proficiency even in one small branch without devoting much time, thought and labour to it. Do not therefore fall in the common error of youth by thinking that life is long and that it could be squandered on aimless occupations. You are a privileged people, who have access to our clinics and our laboratories. When I visit the beautiful institutions and laboratories in your great city, I am reminded of the inspiring words of Louis Pasteur, which I shall now translate for you.

"If the conquests which are useful to humanity touch your heart, if you are jealous of the role of your country in the discovery of marvels of science, I beseech you to take an interest in these sacred buildings which we designate by an expressive term, the laboratories. Ask that they multiply, that they be equipped. These are the temples of the future, its wealth and its well being. It is there that humanity grows, strengthens and betters itself. In them humanity learns to read progress and harmony in the works of nature, whereas, her own works are often barbarous, fanatical and destructive."

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## Critical Notes and Abstracts

### THE TREATMENT OF FILARIASIS WITH LITHIUM ANTIMONY THIOMALATE

This report is based on the treatment of 12 patients infected with filariasis (*Wuchereria bancrofti*) treated during the summer of 1943 with lithium antimony thiomalate. All were natives of St. Croix, Virgin Islands. The results of the therapy were measured by microfilaria counts on 0.1 cc of blood. Since the microfilariae exhibit a nocturnal periodicity, all specimens of blood were drawn from the cubital vein between 10 and 10-30 p.m. All injections of lithium antimony thiomalate were given into the gluteal muscles, alternating sides daily unless the patient complained of soreness on one side. Usually a single daily injection was given on consecutive days unless prevented by poor co-operation of the patient or toxic manifestations of the drug. The adult dose of 3 cc (180 mg) was used adjusted with smaller doses for children. On the first day of treatment of a half-sized dose was given to ascertain sensitivity of the patients to the drug. The microfilaria count of the patients was reduced by this therapy from 85 to 100 per cent as compared with untreated controls. This reduction was maintained for four to five months after completion of treatment and means presumably that a corresponding number of the adult worms were killed. One patient failed to respond to treatment, and there was no reduction in his microfilaria count. No reduction in size of enlarged lymph glands or one enlarged scrotum could be detected four to five months after the completion of treatment. One

patient noted a pronounced improvement in his inguinal distress on exercise following treatment. The patients' history and physical examination failed to reveal any pathologic changes due to the death of the adult worms or microfilariae. It was concluded that the toxic manifestations due to lithium antimony thiomalate of vomiting, joint pain, slight fever and rash are not considered sufficient to preclude its continued trial in filariasis.

(Brown, H W J.A.M.A. 125 952, August 5, 1944)

## **PENICILLIN**

A method of prolonging the action of penicillin, so that gonorrhea can be cured by one dose, has been developed by Captain M J Romansky, U S Army Medical Corps, and G E Rittman, Army Medical Department technician. Instead of giving penicillin in a salt solution, they mix it with U.S.P. bleached beeswax in peanut oil. This mixture delays absorption of the penicillin so that it stays in the blood stream for seven hours, as compared with three hours when given in salt solution. Gonorrhea was cured in 64 patients with one dose each of the beeswax-peanut oil mixture containing penicillin. Fastest gonorrhea cures with penicillin heretofore reported were accomplished in one day but required five large doses for each patient. The new mixture keeps its anti-germ power at room, incubator and refrigerator temperature for 30 to 62 days. It should make penicillin treatment more convenient for both patients and doctors and also make it easier to determine the optimum dose and the period of time necessary for treatment.

## **CUTANEOUS LEISHMANIASIS**

This report from the Medical Corps of the U S Army is based on 499 proved cases of leishmaniasis of the skin in American forces stationed in the Middle East. Cutaneous leishmaniasis is a granulomatous, ulcerative lesion caused by the protozoan parasite, *leishmania tropica*. The disease is endemic in India, Persia, Africa, Iraq, Palestine, countries bordering the Mediterranean Sea, southern Russia, and in Peru and Brazil. The parasite is identical morphologically and culturally with the *leishmania donovani*, the causative agent of Kala-azar. It was found from observations on these cases that neostan (stibamino-glucoside—a pentavalent compound of antimony) given intravenously is a safe drug to use in the treatment of this disease. The average cured case received 1.14 gm of neostan and injections were given twice a week. This was probably too conservative. It is suggested that the same dosage described be used, but that injections be given three times a week. Toxic reactions following neostan intravenous injections can be almost completely abolished by having the individual abstain from food for about five hours before receiving an injection. Only non-infected lesions in accessible regions should be treated by local methods. Any lesion with the slightest evidence of secondary infection must be treated with an intravenous drug. Neostan (2 per cent solution) locally is effective in the treatment of this con-

dition The shortest cure interval (33 weeks) was obtained with this drug Berberine sulfate locally, in the authors' experience, is a relatively ineffective drug Ethyl chloride spray is effective in treating cutaneous leishmaniasis It cures only very early, small lesions The results obtained with superficial x-ray therapy in a small group of cases suggests this is effective in selected cases Only 0.7 per cent of the group had, or developed, a complicating secondary injection Only one case developed a reinfection or recurrence of cutaneous leishmaniasis during this period

(Ball, Major D & Ryan, Captain R Bulletin US Army Med Deptt 79 65, August 1944)

## Book Reviews & Notices

**GALEN ON MEDICAL EXPERIENCE** first edition of the Arabic Version with English Translation and notes by R. Walzer, published for the trustees of the late Sir Henry Wellcome by the Oxford University Press, London, 1944 pp 164 (Arabic Text pp 1-83 Translation 85-155), price 12s. 6d

Galen wrote his *Treatise on Medical Experience* before the year 150 A.D., before he completed his twenty-first year! The original text has been lost, and the earliest version at present known is the ninth-century Arabic translation, discovered in Constantinople by Riter in 1931 The philosophical and historical importance of the treatise has led the Trustees of the late Sir Henry Wellcome to publish the text of the Arabic version together with the English translation and notes by R. Walzer The Arabic translation by Hubais, from the Syriac translation by Hunain from the original Greek, is considered to be of an exceptionally high standard, giving new proofs of Hunain's astonishing command of the Greek scientific language The treatise is of importance for the history of the Sceptics in general, as well as for its bearing on our knowledge of empirical and dogmatic medicine It contains a new fragment of Demokritos, and mentions Diogenes (of Apollonia) as a physician Galen intended this treatise as an aid for beginners to the understanding of his previously written work In the polemical discussion between the Dogmatist and the Empiricist, the latter wins the day in the warfare of words and establishes his case for the union of Empiricism and Theory which Galen determinedly affirmed all his life Galen ends the argument with "To sum up, in our argument we demonstrated that experience suffices to discover the things used in healing"

**YOUR FOOD** by M. R. Masani, published for Tata Sons Ltd., by Padma Publications Ltd., Bombay, 1944, pp 82, Re 1

This small pamphlet is the first of a series of publications sponsored by Tatas to stimulate interest in some of the vital problems facing India The subject of food is of perennial interest in India—the land of famines, perpetual hunger, and peculiar food habits Mr Masani is not a physiologist, nor a physician, but a politician and a popular writer, and has written a booklet which will appeal to school children by its simple and clear presentation of facts, for which he has taken

technical assistance of W R Aykroyd of Coonoor The illustrations by A R Acott are a special feature of the book and require a special word of appreciation We have nothing but praise for this modern educator, and do not hesitate to recommend its use as a compulsory reader for all school children and social workers

**THE 1944 YEAR BOOK OF GENERAL MEDICINE**—edited by G F Dick (Infections), J B Amberson (Diseases of the chest excluding the heart), G R Minot and W B Castle (Blood and Kidney), W D Stroud (the Heart and Blood vessels) and G B Lusterman (Digestive system and Metabolism) Published by The Year Book Publishers, Inc., 304 South Dearborn Street, Chicago pp 768, price 3 U.S.A. dollars

This volume is one of the 12, comprising the Practical Medicine Series of Year Books founded in 1900 by G P Head and C J Head and published continuously since then The series has established its place in the medical world and is read all over the world, because of the high position held by its editors, who are men of international repute, and whose selection of articles for abstract being marked by high standard and discrimination The editorial critical notes at the end of many abstracts are highly instructive and the editors do not hesitate to say so if they differ from the author of the article in fundamentals The articles are abstracted from journals of all countries and no library or practitioner desirous of being in touch with the current literature should be without this series of handy volumes

## Reflections & Aphorisms

¶The attitude of the patient approaching his doctor must always be tinged—for the most part unconsciously—with distaste and dread, its deepest desire will tend to be *comfort and relief rather than cure*, and its faith and expectation will be directed towards some *magical exhibition of these boons* Do not let yourself believe that however smoothly concealed by education, by reason and by confidential frankness these strong elements may be, they are ever in any circumstances altogether absent

—WILFRED TROTTER, F.R.S.

¶Do not arrogate to yourselves a knowledge which you do not possess, do not be afraid to say you do not know, do not hesitate to ask for a little time to think things over In issues involving life and death one could not afford to be casual or thoughtless, though an emergency might sometimes compel one to act promptly For the young doctor "*sense*,"—*implying exactness and soundness, power and promptitude of mind*—*must be the master faculty* But he must have *genius too, a real turn for his profession, and presence of mind* How man lived, moved, and had his being was still an unsolved mystery, but one can be certain that he should not be thought of as a stomach, heart, lungs, or bowels, but as a whole personality His likes and dislikes, his loves and hates, fears and hopes, his aspirations and disappointments might supply the key to his more mundane complaints

—D K HENDERSON

# The Indian Physician

VOL IV NO 5

MAY 1945

WHOLE NO 41

## Original Contributions

### BENIGN EOSINOPHILIA WITH PULMONARY SHADOWS

NATHOOBHAI D. PATEL,

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K. E. M. Hospital & G. S. Medical College, and P. G. S. Hindu Hospital, Bombay

Since 1931 I have observed in Bombay cases of eosinophilia associated with pulmonary roentgen shadows which are non-tubercular and which run a benign course. My first case was that of a lad of 14 who was pronounced to be suffering from miliary tuberculosis because of the x-ray appearances. He had a history of a few days' fever, spasmodic cough and some loss of weight. The sputum on repeated examinations had failed to show tubercle bacilli. The blood had showed leucocytosis and eosinophilia but the pulse rate was normal. Knowing that some cases of whooping cough showed an x-ray picture similar to that of miliary tuberculosis, I considered the condition to be most probably benign. He recovered without any special treatment and has been quite well all these 14 years. Frimodt-Møller and Barton (1940) were the first to record the association of eosinophilia with non-tuberculous pulmonary lesions in sanatorium patients in South India, calling it a "pseudo-tuberculous condition associated with eosinophilia." The extensive mottling of small nodular shadows over both lung fields was considered by them to be non-tubercular and probably of allergic origin. Weingarten (1943) together with Berger observed during the years 1934-1941, 81 cases of massive eosinophilia with pulmonary symptoms and signs in persons of all communities coming from the Western Coast of India. Since his first record he has observed further 45 cases during 1941-1943. He calls the condition '*Tropical Eosinophilia*', '*a new disease entity, apparently peculiar to certain parts of India*'. He has given a complete clinical picture and a specific remedy in arsenic. Similar cases have also been observed by Treu (1943, 1944), Simeons (1943), Owen (1943, Eosinophilic Lung), Hellig and Visveswar (1943), Vaidya (1943, a record of 6 cases from many seen during the years 1929-1934 and all treated with neo-salvarsan), Patel (1943, 6 cases, 1944,

A paper read at the 40th Scientific Meeting of the G. S. Medical College and K. E. M. Hospital Staff Society, Bombay, on March 10, 1945, with Dr. V. R. Khanolkar, M.D. (Lond.) in the Chair.



1 case), Parsons-Smith (1944), Chaudhari (1943), Roy Sudhir (1943), Shah (1943), Emerson (1944), Leishman and Kelsall (1944—7 cases), Apley and Grant (1944), Carter, Wedd, and d'Abrera (1944—3 Ceylon cases where mites were observed in the sputum which were considered to be of etiologic significance) and Soysa and Jayawardena (1945, detailed report of 30 cases seen in Ceylonese soldiers where mites were found in the sputum in 11 out of 21 cases whose sputum was examined by the special technique) Similar cases are also recorded from the Madras Presidency, Behar and the United Provinces From our institution a case, observed from 25-5-1934 to 4-7-1935 and recorded by Hamid (1935), where the leucocyte counts ranged between 31,300 and 50,000 per c mm with eosinophil percentage of 69 to 87, was probably of similar nature

I have notes of 49 cases personally seen by me from 1-10-1943 to 30-11-1944, a period of 14 months Most of these cases were seen in private consulting practice and only a few in the out-patients department of our hospital This is because most of the cases with cough attending the out-patients department are dismissed with that panacea of the out-patients' physician, mist expectorans or mist anti-asthma, and routine blood examination is not carried out This large number of cases seen by one individual in a short period, taken together with the number of cases not diagnosed because of absence of blood examination, will give one some idea about the very common prevalence of the malady

The essential details such as age, sex, race, occupation, residence, total white cell count with eosinophil percentage and other physical finding of the 49 cases observed by me are given in Table No 1

#### GEOGRAPHICAL DISTRIBUTION

All my cases were from the Province of Bombay, except two, one from Madras and one from the United Provinces Of the Bombay cases, 10 were from the City of Bombay and 28 from the suburbs, most of them coming from Ghatkopar, Vile Parle and Matunga Nine were from Surat and Kaira districts Weingarten has observed that all his cases were persons living near the sea, on the Bombay, Gujarat, and Kathiawar coast and on the Malabar and Coromandal coasts except 3 who lived inland but often used to visit or stay near the sea He has seen no cases in a stationary population in the interior of India with a dry climate with extremes of summer and winter He reports one case from the United Provinces of a girl who lived for some years in a swampy area Most of the cases reported by others are also from the coastal areas of India The influence of environment as an etiologic factor is therefore unquestionable

#### SEX

Of these 49 cases, 37 were males and 12 females The higher number of males is probably due to a larger number of males seeking medical advice or leading a more exposed life, and does not suggest sex as an etiologic factor,

TABLE I  
CASES OF EOSINOPHILIA SEEN FROM 1-10-1943 to 30-11-1944  
M Male F Female, H Hindu, RC Christian M Moslim HW Housewife

Case	Date	Name	Age	Sex	Comm	Occu	Resi	Total White Cell Count	Eosin ophil per cent	X Rays	Lymph Nodes	Spleen
1	1-10-43	RP	25	M	H	Clerk	Mahim	12,500	24			
2	2-10-43	RI	15	M	H	Study	Ghatkopar	38,500	74	+	+	
3	28-10-43	RC	56	M	RC	Clerk	Bandra	12,500	15			
4	11-11-43	GC	24	M	H	Clerk	Madras	19,000	24		+	
5	11-11-43	RH	22	M	H	Merchant	Ujjaini U P	21,000	30	+	+	
6	15-11-43	SD	25	M	H	Doctor	Girgaon	27,000	56			
7	20-11-43	S	35	M	H	Doctor	Dadar	32,000	68			
8	20-12-43	MD	16	M	H	Study	Olpad Surat	21,200	72	+	+	+
9	4-1-44	M	31	F	H	Housewife	Girgaum	14,350	10			
10	8-1-44	VC	12	M	H	Study	Surat	32,000	70			
11	10-1-44	SB	8	M	H	Study	Surat	29,000	54	+	+	+
12	11-1-44	CG	39	M	H	Merchant	Broach	19,000	26			
13	20-1-44	SB	30	M	H	Coolie	Malad	22,000	60	+	+	+
14	12-2-44	DH	12	M	H	Study	Ghatkopar	28,000	35	+	+	+
15	15-2-44	MBP	10	M	H	Study	Ghatkopar	19,200	43	+	+	+
16	25-2-44	SS	9	M	H	Study	Lohar Chawl	12,200	17			
17	1-3-44	PC	9	M	H	Study	Ghatkopar	13,000	48	+	+	
18	10-3-44	DD	19	M	H	Merchant	Ghatkopar	18,000	35			
19	18-4-44	PP	16	F	HW	HW	Vile-Parle	28,000	68	+	+	
20	2-5-44	SP	35	F	H	HW	Vile-Parle	32,200	64	+		
21	2-5-44	VP	10	M	H	Study	Vile-Parle	9,800	9			
22	6-5-44	BD	72	M	H	Timber Mer	Bulsar	19,000	16			
23	8-5-44	GHC	9	M	H	Study	Ghatkopar	18,000	46	+	+	+
24	15-5-44	BK	72	M	H	Merchant	Ghatkopar	23,500	52	+	+	
25	15-5-44	MK	35	M	H	Merchant	Ghatkopar	22,000	42			
26	18-5-44	PP	26	F	H	HW	Matunga	14,000	25			
27	26-5-44	Q	15	M	M	Study	Byculla	14,900	33	+	+	
28	0-6-44	MD	30	M	H	Clerk	Thakurd	15,200	21			
29	12-6-44	UBP	41	M	H	Agricult	Anand	9,000	19			
30	18-6-44	VIM	28	M	H	Clerk	Shivaji Pk	42,350	68	+	+	
31	23-6-44	VJT	28	M	H	Hardware	Ikar	29,000	81	+	+	
32	26-6-44	D	24	F	H	HW	Bulsar	39,000	74	+	+	
33	30-6-44	MR	20	F	RC	HW	Bandra	12,000	45	+	+	
34	2-7-44	M	22	F	H	HW	Girgaum	41,360	74	+	+	
35	14-7-44	D	24	F	H	HW	Vile Parle	10,000	19			
36	10-7-44	DS	9	F	H	Study	Chatkopar	25,600	50			
37	21-7-44	DM	40	M	H	Teacher	Matunga	18,240	63			
38	10-8-44	AD	8	M	H	Study	Marine Drive	9,000	15	+	+	
39	18-8-44	KM	48	M	H	Merchant	Andheri	19,000	68			
40	18-9-44	SLM	40	M	H	Doctor	Ghatkopar	21,800	52			
41	1-10-44	Sav	15	F	H	HW	Vile-Parle	34,600	63	+	+	
42	10-10-44	R	16	F	RC	HW	Bassein	28,000	48	+	+	
43	30-10-44	MM	32	M	H	Pleaser	Tardeo	11,600	11			
44	31-10-44	IICM	11	M	H	Study	Matunga	19,200	56	+	+	
45	9-11-44	JK	11	M	H	Study	Matunga	17,800	17			
46	7-11-44	RCD	17	M	H	Agricult	Chikili	16,000	41			
47	17-11-44	S	27	F	H	HW	Null Bazar	15,000	32			
48	24-11-44	C	35	M	RC	Priest	Bandra	29,000	51			
49	29-11-44	SR	42	M	H	Merchant	Ghatkopar	12,200	17			

## AGE

The youngest patient in this series is 8 years old, who had symptoms and signs since the age of 3, and the oldest 56 years. There are only 6 cases under the age of 10 and only 6 after the age of 40. The largest number, 37, being from 10 to 40, the distribution between the three decades being roughly equal. The highest incidence is thus in youth and adult life. In Weingarten's series also the highest incidence was in the age-group 15 to 45.

## RACE

Almost all of my cases were Hindus, only three being Christians, and only one a Mohammedan. This is due to the nature of Bombay practice, and has no bearing on the etiology of the condition. The syndrome is recognised in all communities and races in India, even in visitors such as Europeans, Arabs, Americans, and others.

## SEASON

As most cases are diagnosed late during the chronic stage it is difficult to correlate its incidence with seasonal variations. Early cases seeking advice are rare and often misdiagnosed.

TABLE 2

AGE	1 to 9	10 to 19	20 to 29	30 to 39	40 to 49	50 to 59	60	Total
	0	14	12	11	5	1	0	40
SEX:	Males 37		Females: 12		40			
COMMUNITIES:	Hindus 44,		Moslims: 1,		Christians 4		40	
LOCALITY								
Bombay City 10	Bombay Subs 28		South Gujarat: 0		Outside Bombay Presidency 2		40	
MONTHLY INCIDENCE								

A collection of a large number of cases, in acute or subacute stages and also relapses and exacerbations in chronic cases, noting if they bear any relationship with any flowering plants or trees in the locality, or with the breeding of any likely vector, will certainly be a fruitful investigation. At present it appears that seasonal variations play no role in the etiology of the malady, except that in chronic cases attacks of asthma are frequent during monsoon and after exposure to cold winds.

## OCCUPATION, SOCIAL STATUS, FOOD HABITS, SMOKING, AND ALCOHOL

None of these appears to have any importance in the production of the syndrome. Most of my patients have been middle class Gujaratis, either clerks, or petty businessmen, farmers, doctors, pleaders, housewives and students. There are no workers from the Bombay cotton mills. Only two had anything to do with dyes, case 4 is a clerk in a company dealing with dyes and has to handle samples, and case 41 is a daughter of a man occupied in the cloth-printing-by-hand business who keeps stock of dyes in his house.

## ALLERGY

Of constitutional susceptibility and family history of allergy, though it is difficult to obtain reliable information from our patients, it is possible in some cases to establish a family or personal history of allergy. Weingarten stated that there was "no familial or constitutional susceptibility and more than one case was not observed by him in one family, however large." This is not my experience.

The very first case I saw in 1931 gave a strong history of allergy in the family, grandmother suffering from migraine, father from migraine and Meniere's disease, and a sister from urticaria and gastro-

intestinal allergy The first case recorded by Heilig had a brother suffering from migraine In this series case 10 is the son of a doctor who had himself asthma-like attacks during 1932-33 which he got treated with two injections of neosalvarsan At present he is free from all symptoms but his blood count shows 9000 white cells with 9 per cent eosinophils Constitutional allergic factor is well illustrated by cases 19, 20 and 21 of this series Case 20 is the mother suffering from asthma-like attacks for the last 15 years, while cases 19 and 21 are her daughter and son who have developed the malady during last two years Incidentally the case 19 is the only one of this series who developed severe arsenical dermatitis after the 6th injection of neoarsphenamine and the case 20, the mother, was so sensitive to arsenic that after the first dose of 0.15 gm neoarsphenamine she had a severe reaction vomiting, pruritis, and fever lasting for 3 days Carbarsone by mouth also produced gastrointestinal symptoms and had to be omitted Case 33 has a sister suffering from chronic asthma and case 41 has a mother with eczema

#### THE CLINICAL PICTURE

The clinical picture presented by these cases is so characteristic that no separate individual description of case histories is considered necessary Apart from minor variations most cases confirm to a type which is easy to recognise clinically The duration of the disease varied from a few weeks to several years

In most cases the *mode of onset* was slow and insidious A few gave a history of *fever* lasting for a few days at the onset, or irregular fever for a day or so during the course, in others the course was entirely afebrile The fever at the onset was sudden, with headache, marked prostration, and muscle pains At first there was only leucocytosis, with slight increase in eosinophils It was only after a week or fortnight that massive eosinophilia appeared Unusually the fever may be prolonged to 2 or 3 weeks During this stage a variety of diseases e.g., typhoid, tuberculosis or broncho-pneumonia following measles, etc., are thought of In the chronic stage, which followed after a lag of some days, the chief complaints were (1) *cough*, (2) *asthma-like attacks*, (3) *loss of weight*, and (4) *loss of energy* The cough was dry, hacking, and ineffective It was paroxysmal and worse at night, especially in the early hours During the day there was freedom from cough The sputum, if any, was scanty and brought out with great difficulty The paroxysms of coughing later became more frequent, followed by wheezing and expiratory dyspnoea In some cases typical attacks of *bronchial asthma* occurred regularly, sometimes after midnight or in the early hours of the morning These attacks may persist for several weeks or even years The paroxysms of coughing in some patients ended with vomiting The attacks were sometimes brought on by exposure to cold, mental upsets, or by eating some particular food The appetite was poor after sleepless nights and the fear of nocturnal attacks or vomiting made the patient afraid of eating The *loss of weight* which was considerable at the beginning of the illness became

more marked as the patient experimented with dieting. After a month or two of cough and asthma *general weakness and easy exhaustion* appeared. In a few cases there was arrest or spontaneous recovery, the weight becoming steady, the cough disappearing and the general health and energy becoming normal. In most other cases, though the progressive loss of weight stopped and the lassitude decreased, the paroxysms of coughing and the asthma-like attacks at night persisted and the condition became *chronic*.

The physical examination showed the usual *signs of asthmatic bronchitis*,—hyperresonance of the chest, prolonged expiration with sibilant and sonorous rhonchi all over the chest, and coarse râles at the bases. The *sputum* if any was scanty, white, glaring and viscid. The *spleen* was palpable in only 4 cases of this series. This is because perhaps all these cases were chronic cases. Weingarten has observed a moderate enlargement of the spleen, 3.5 cm. below the costal margin, during the febrile period. Splenic enlargement was not observed, also in the series recorded by Soysa and Jayawardena (1945). *Enlargement of the lymph nodes* was seen frequently by me in this series. As many as 22 out of 49 cases showed palpable lymph nodes in the posterior triangles of the neck and in the axillae. These were hard, discrete, not tender and variable in size. They disappeared very gradually under treatment. One patient, case 2, had *bilateral swelling of the parotids* which looked like mumps and which subsided after arsenical treatment. The *liver* was not enlarged in any case. There was no evidence of disease in alimentary, cardiovascular, genito-urinary, or nervous systems. Evidence for other allergic manifestations in these patients, except for repeated attacks of cold or vasomotor rhinitis, was entirely lacking.

Some patients with eosinophilia were suffering from other diseases, not related in any way to it. Thus case 40, had spastic paraplegia, macrocytic anaemia and signs of pellagra, case 24 had schizophrenia of long duration and was under shock treatment with cardiazol, when eosinophilia and enlargement of the lymph nodes were discovered on routine examination. Case 20 was a subject of congenital mental deficiency. I have previously (1944) reported a case of patent interauricular septum, with marked eosinophilia.

#### LABORATORY INVESTIGATIONS

The *blood examination* showed massive eosinophilia with leucocytosis. The highest count observed in this series was 42,350 white cells, with 68 per cent or 28,832 total eosinophils per c.mm. The highest eosinophil percentage in this series was 81, with 23,500 total eosinophils. The highest count in Weingarten's series was 74,000 total leucocytes and eosinophilia upto 89 per cent. As high as 87 per cent eosinophilia has been observed by Vaidya (1943). The absolute number of neutrophils and lymphocytes were not proportionately affected. The eosinophils were normal in size, shape, and staining properties, and fully mature. The red blood cells and haemoglobin were normal in most cases, some showed a mild degree of secondary anaemia, a few

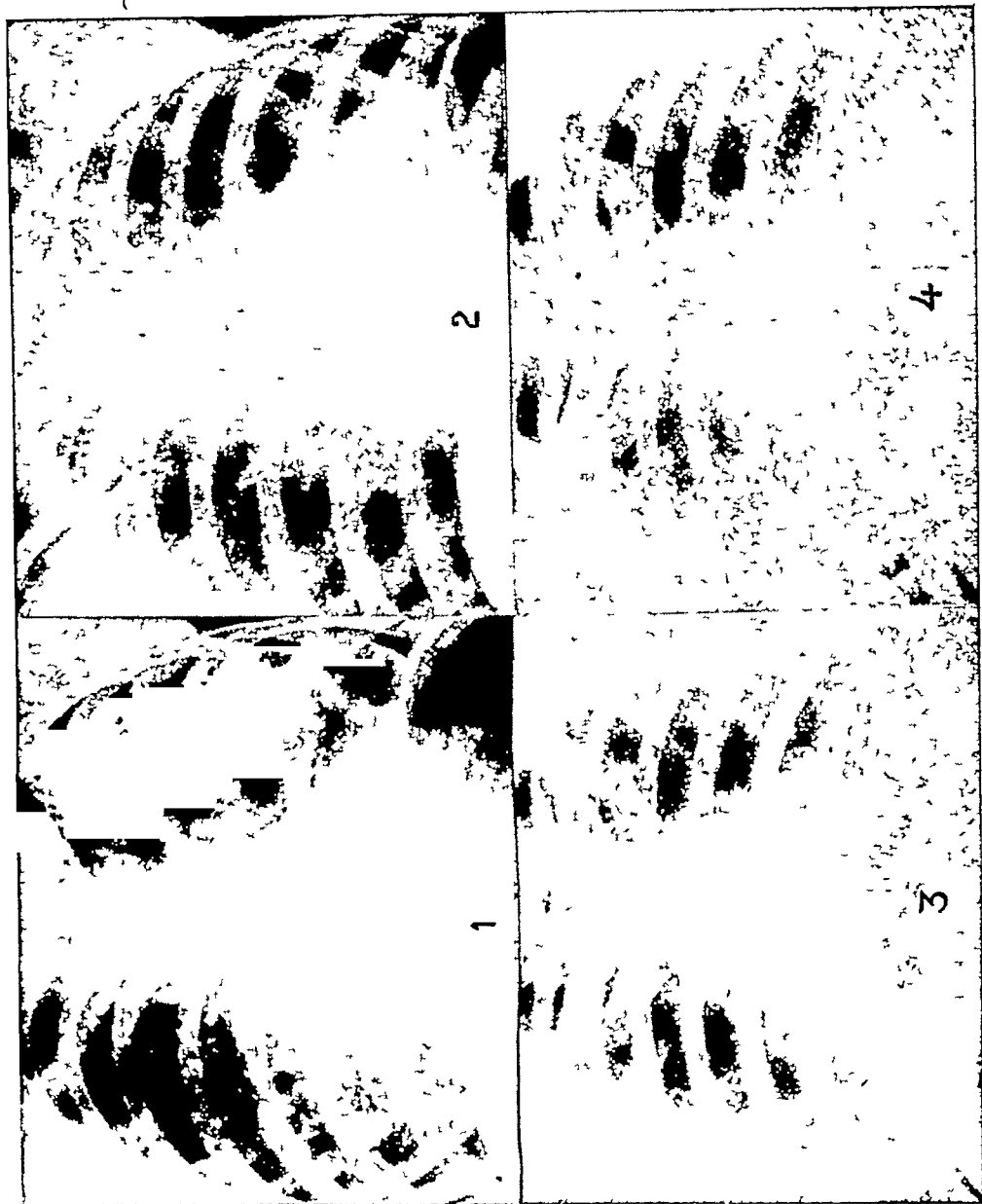


Fig —1 X ray plate of Case No 2 before treatment. Total White Blood Cells 38,500 per cmm Eosinophils 74 per cent.

Fig —2 Same Case after treatment Total White Blood Cells 8,800 per cmm Eosinophils 22 per cent

Fig —3 X ray plate of F (Dr Raghavan's Case) before treatment Total White Blood Cells 41,000 per cmm Eosinophils 75 per cent.

Fig —4 Same Case after treatment. Total White Blood Cells 14,050 per cmm Eosinophils 22 per cent

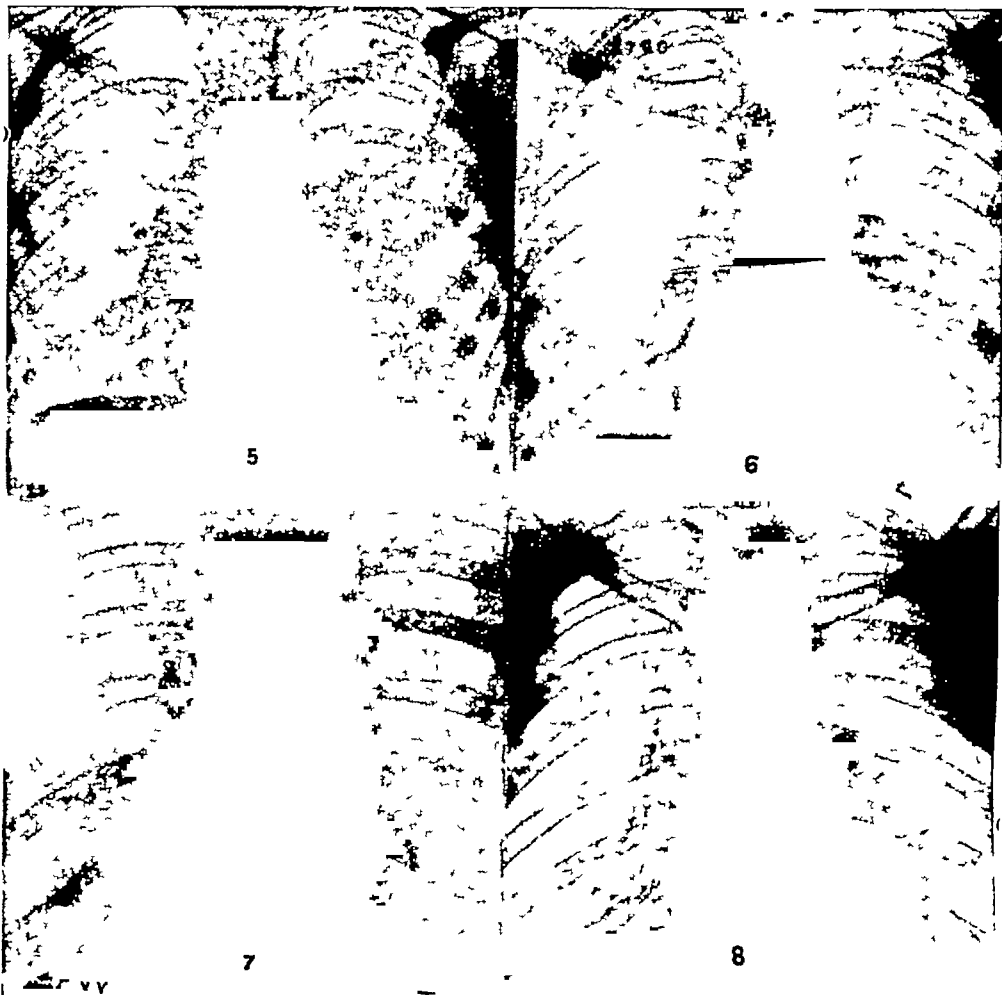


Fig.—5 X ray plate of Case No 4 Total White Blood Cells 28,000 per cmm Eosinophils 38 per cent.  
Fig.—6 X ray plate of Case No 5 Total White Blood Cells 21,000 per cmm. Eosinophils 30 per cent.  
Fig.—7 X ray plate of Case No 30 Total White Blood Cells 42,350 per cmm Eosinophils 63 per cent.  
Fig.—8 X ray plate of Case No 24 Total White Blood Cells 23,500 per cmm Eosinophils 52 per cent

had a high red cell count between 5 and 65 million per c mm and haemoglobin percentage between 100 and 110 (Sahli). No parasites or immature cells were seen. One case was suffering from macrocytic anaemia and spastic paraplegia (case 40) and he had a blood picture typical of that disease.

The erythrocyte sedimentation rate was noted in a few cases and it was found to be raised, 25, 44, 67, 86 mm per hour. Casoni intradermal reaction, tuberculin patch test and search for filaria were all negative. Kahn test was positive only in one case which became negative after a course of treatment with arsenic.

As most of these were my private room patients routine examinations of stool and urine were not possible. Of those in the hospital the urine showed no abnormality on routine chemical and microscopic examination. The stool examination showed cysts of *Entamoeba histolytica* in two cases and no other abnormality. The usual parasitic infestations of the tropics, *Ancylostoma duodenale*, *Ascaris lumbricoides*, *Trichuris trichura*, *Blastocytis hominis*, *Trichomonas faecalis*, have been observed by the Ceylon workers who report that the appropriate anthelmintic treatment had no effect on the eosinophil counts, and were thus without any etiological significance. The sputum examination showed clumps of eosinophils, a fair number of lymphocytes and epithelial cells, Charcot-Leyden crystals, or spirals on routine examinations. No special examinations were carried out for spirochetes in the sputum or for mites in the sputum, urine or faeces.

#### SPECIAL INVESTIGATIONS

Sternal punctures were performed in 7 cases (Nos 8, 13, 24, 27, 30, 33, and 41), and lymph nodes were removed for biopsy in 5 cases (No 8, 13, 24, 30 and 41). Sternal fluids and lymph nodes were kindly examined for me by Dr V R Khanolkar of the Tata Memorial Hospital. The sternal fluids did not show anything abnormal except marked myeloid reaction. The lymph nodes also did not show anything abnormal, except subacute lymphadenitis. Eosinophilic infiltration was not seen. The results of animal inoculations with citrated blood were entirely negative.

#### X-RAY APPEARANCES

The x-ray appearances were quite typical. These were best seen in a film and not so well on screening. There was an increased linear striation of the finer lung marking, symmetrically distributed in both lung fields, suggesting a bronchitic or bronchiolitic reaction. Also, there were numerous round, ill-defined, discrete shadows, scattered throughout both the lungfields, especially in the basal and hilar regions, which produced a peculiar mottled appearance. These shadows were marked and best seen in early cases, but were also present in chronic cases of several years' duration. The extent of the lung shadows could not be correlated with the blood eosinophilia or with the clinical symptoms. The opacities and the linear shadows disappeared spontaneously in some cases or, on arsenical treatment, as the blood eosinophils returned to normal (15 x-ray films were shown to illustrate



these points, of which a few are reproduced on the plates facing pages 98 and 99)

#### DIAGNOSIS

The diagnosis is made from the typical clinical picture, high leucocyte count and eosinophilia. *In every case of chronic cough with loss of weight and asthma-like attacks, total and differential white cell count should be carried out and a skiagram taken.* Leucocyte counts above 15,000 per cmm and eosinophil percentage above 20, or a total eosinophil count above 3000 per cmm is diagnostic of this syndrome and should exclude other conditions causing eosinophilia in Bombay. The higher the leucocyte and the eosinophil count, the more certain the diagnosis. It must be remembered that the blood eosinophils may spontaneously fluctuate without any treatment, so that if the eosinophil percentage is low with a typical clinical history, the blood examination should be repeated after a time or a therapeutic test carried out. The x-ray appearances are typical but they may be absent, even in the presence of marked subjective symptoms, or a very high blood eosinophilia.

In differential diagnosis one has to consider other causes of (1) asthmatic bronchitis, (2) eosinophilia, and (3) pulmonary shadows.

In classical bronchial asthma high leucocytosis is rare, and the eosinophil count is rarely very high. The paroxysms of dyspnoea are very severe, with marked anxiety, restlessness and sense of suffocation.

The allergic bronchitis resulting from inhalation of house dust, fungi, yeast,orris root, different foods, bacteria etc., will also produce a high eosinophil count upto 10-20 per cent and the differential diagnosis at times is difficult. The history of allergy in the family and perennial rhinitis and other allergic manifestations in the patient should be taken into consideration. Ultimately, the diagnosis is made by eliminating all other possibilities.

The eosinophil count is high in allergic states produced by roundworms, filaria, trichiniasis, liver-flukes, brucella infections, echinococcus, amoebiasis with liver abscess, and gastro-intestinal allergy. In skin diseases, such as eczemoid neurodermatitis, pemphigus vegetans, dermatitis herpetiformis, or psoriasis, the eosinophils may be increased but are rarely very high and will probably give no difficulty in diagnosis.

Eosinophilic leucaemia and constitutional or hereditary eosinophilia are ill-defined terms and as Heilig (1943) has suggested both these conditions are overlapping syndromes with benign eosinophilia. The eosinophil count may also be high in lymphogranuloma, states of vascular allergy and periarteritis nodosa, malignant involvement of the pleura or peritoneum, secondary to ovarian carcinoma.

Stickney and Heck (1944) state that clinically, eosinophilia is a common finding in

- (1) asthma hay fever and vasomotor rhinitis
- (2) parasite infestations especially those of the intestine
- (3) dermatoses especially the type in which allergy plays a role and
- (4) blood dyscrasias and lymphoblastoma.

Eosinophilia is occasionally observed in—

- (5) non parasitic infections, e.g. appendicitis, chronic ulcerative colitis, cholecystitis, rheumatic arthritis,

- (6) malignant lesions of all types, especially with liver metastases;
- (7) periarthritis nodosa,
- (8) post febrile debility;
- (9) starvation,
- (10) syphilis
- (11) administration of digitalis,
- (12) polymyositis
- (13) pleural effusions
- (14) benzene and nirvanol poisoning and
- (15) ingestion of raw liver, or injections of liver extracts

Stickney and Heck have analysed a group of 418 cases in which 6 per cent or more of the leucocytes in the blood stream were eosinophils. In their opinion, the degree of eosinophilia is of little importance in differential diagnosis. Eosinophilia in excess of 20 per cent would seem to have little more significance than eosinophilia of a lesser degree except that the possibility of periarthritis nodosa or a blood dyscrasia being present may be greater in the presence of the higher percentage of eosinophils. The daily, and perhaps hourly, variation in the eosinophils is considerable and may alter the importance of the findings.

DISEASE PRESENT AND PERCENTAGE OF EOSINOPHILS IN THE CIRCULATING BLOOD IN 418 CASES IN WHICH EOSINOPHILIA WAS PRESENT (Stickney and Heck)

Disease	Per Cent of Eosinophils		
	6 to 10	10 to 20	20+
	(Per cent of cases)	(Per cent of cases)	(Per cent of cases)
Asthma hay fever and vasomotor rhinitis	33	44	28
Non parasitic infections	10	12	11
Blood dyscrasias and lymphoblastoma (leukemia excluded)	5	8	20
Dermatoses	7	0	10
Parasitic infections	5	3	4
Malignant lesions	5	8	4
Periarthritis nodosa			10
Miscellaneous	31	21	13
Total	100	100	100

The pulmonary shadows in the skiagrams have to be differentiated from similar shadows produced in *miliary tuberculosis*, *pulmonary congestion in cardiac failure*, *miliary and submiliary densities in rheumatic mitral stenosis*, *sarcoidosis*, *pneumonoconiosis*, *virus pneumonia*, *broncho-mycosis* and *carcinomatosis*. Hansen-Fruss and Goodman (1944) have discussed the differential diagnosis of allergic pulmonary consolidations. These authors believe that the condition is an expression of sensitization to non-specific bacteria and that it can occur in constitutionally allergic individuals as well as in those who acquire the allergic response.

#### COURSE

The syndrome is essentially benign and may last for several years. Case 37 had asthma-like attacks for the last 17 years, case 20 for 15 years, and case 23 for 6 years. Weingarten reports a case who suffered for over 22 years, had 42,000 white blood cells with 64 per cent eosinophils when came under observation and who made complete recovery on arsenical therapy.

#### RELAPSES

Weingarten has stated that "The fact that not one patient treated with neoarsphenamine or acetylarsan ever returned for advice seems

a proof that no relapse occurred" That relapses do occur is shown by case 6 reported by Vaidya (1943) This patient, a leading surgeon in Bombay had his first attack in October 1934 with a total count going upto 60,000 and eosinophils upto 87 per cent He recovered after six injections of neosalvarsan and remained well for *three and a half years* when he had his *first relapse* in March 1938 with 28,000 white cells and 65.5 per cent eosinophils He recovered after five injections of neosalvarsan and remained well till his *second relapse* which strangely enough followed after three and a half years in October 1941 This time four injections of neosalvarsan brought the count down to normal He had temperature and a high leucocyte count with 1600 eosinophils in September 1943, which he considered to be the beginning of the *third relapse* and aborted it by taking an injection of 0.3 gm neosalvarsan The case I am presenting here, S, Case 41, came under observation

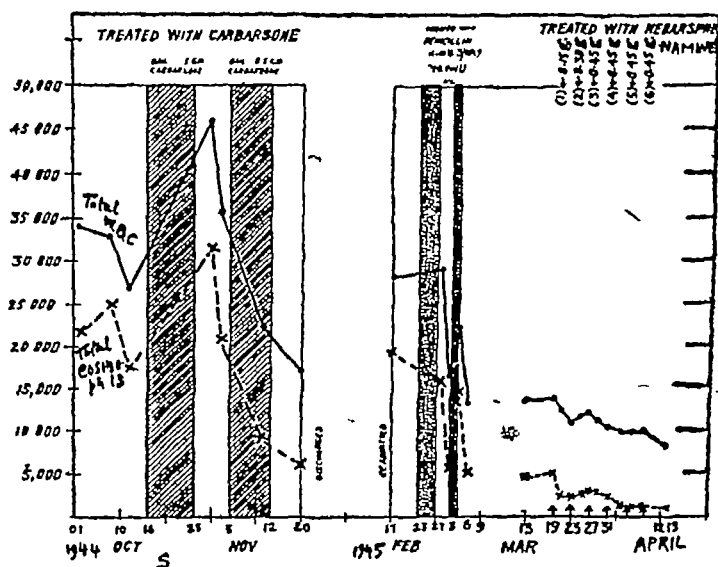


Fig 1 (Case 41) Showing the effect of treatment with carbarsone and nearsphenamine on the White Blood Cells and eosinophils

in October 1943 with 34,600 leucocytes and 63 per cent or 21,798 eosinophils She was treated with two courses of carbarsone She made a good clinical recovery, her symptoms disappearing completely, and her weight going up from 75 lbs to 84 lbs Her erythrocyte sedimentation rate which was 86 mm per hour fell to 25 mm per hour Her blood count on November 11, 1944 was 16,500 total white cells and 36 per cent or 5,940 eosinophils, showing that there was no haematological recovery She was discharged in the hope that the blood condition will keep on improving as she had two courses of carbarsone Within three months on 17th February 1945 she returned with all her symptoms and a blood count of 28,100 white cells and 67 per cent or 18,800 eosinophils The fluctuations in her blood count in the hospital are shown

in the chart, (Fig 1) Penicillin had little effect on her blood condition. Ultimately she made a complete clinical and hæmatological recovery after six injections of neosarsphenamine.

# TREATMENT

Arsenic has been used in the treatment of asthma for a long time, but in Bombay neosalvarsan also seems to have been in use for a long time. Who started its use, I do not know but when I started practice in Bombay in 1930, I found that many practitioners were using neosalvarsan or sulpharsenol freely in all cases of asthma. Many had gained reputation as asthma specialists who without divulging the fact gave three weekly injections of neosalvarsan followed by injections of own blood. Patients came from far and wide and some took these injections every three years. We notice Valdia (1943) recommending the injection of neosalvarsan in 1929. Weingarten has shown that it is a specific for cases of what he calls Tropical Eosinophilia only and not a panacea for all types of allergic bronchitis, or bronchial asthma. He has also shown that organic aromatic arsenicals, neosalvarsan, mapharside, sulpharsenol, acetylarsan, carbarsone, stovarsol, given intravenously, intramuscularly or orally are equally effective.

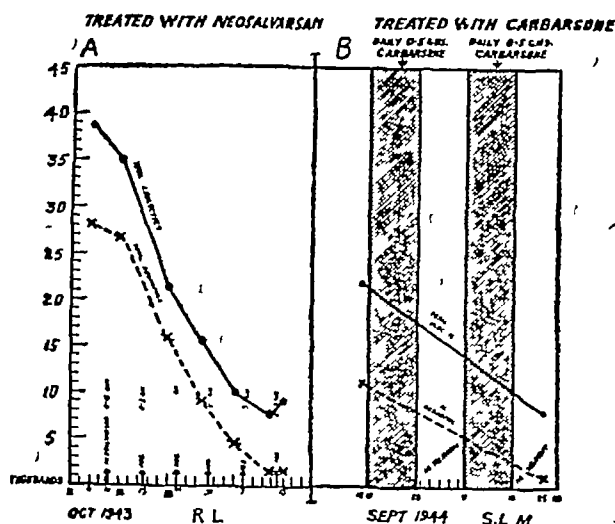


Fig 2 A (Case 2) Effect of Treatment with Neosalvarsan B (Case 40) Effect of Treatment with Carbarsone, on total leucocytes and eosinophils

A course of six injections is given in increasing doses of 0.15g, 0.3, 0.45, twice or thrice, every 4th or 5th day. Weingarten advises the drug to be dissolved in 10 c.c. of 10 per cent calcium gluconate, to which 200 mgm (2 c.c.) of vitamin C are added. After the first or second injection there is a flare up, the subjective symptoms become marked and the total whites and the eosinophil percentage increase in number, and in some cases there is fever 101° to 104° F which may persist for 3 or 4 days. After the next injection there is sudden relief.

from symptoms and the blood count begins to fall. The weight begins to increase and the patient feels as never before. In some cases, the improvement after a single injection of neosalvarsan is striking and the patient fails to turn up for further treatment. The necessity of completing the treatment must be impressed on the patient as the insufficient treatment is likely to produce incomplete recovery, and a chronic state. After six injections the total white cell count falls under 10,000 and the eosinophil percentage under 10. In some cases the fall in the blood count is very rapid, in others slow and may return to normal some weeks after the course is over.

When arsenicals are used by mouth a *similar flare up* occurs after 4 to 6 tablets of carbarsone of 0.25 gm each, or of stovarsol of 4 grains each. Two courses of oral treatment are necessary, lasting for ten days each, with ten days' interval between. The oral treatment is as effective as the injections, less troublesome and time saving.

The changes occurring in blood counts and in weight under treatment are shown in Tables 3, 4, 5, 6 and 7, and in Figs 1 and 2.

TABLE 3

Case 2 R L (15), Lymph nodes+, Parotids+, X ray shadows+, Spleen not palpable (Fig 2A)

Date	Treatment	Total Leuco cytes	PERCENTAGE						Weight
			Eosino phils %	Total Eosin	Neutros	Baso	Lympho	Large Mono	
6-10-43	0.15 gm Neosalvarsan	38,500	74	28390	7	0	18	1	75 lbs
10-10-43									
12-10-43	0.08 gm	35,000	75	26600	7	0	16	1	
17-10-43									
22-10-43	0.03 gm	21,700	75	16275	3	0	22	0	
24-10-43									
29-10-43	0.03 gm	15,600	57	8892	17	0	25	1	80 lbs
31-10-43									
5-11-43	0.03 gm	10,000	45	4500	17	0	32	0	
7-11-43									
12-11-43	0.03 gm	7,700	25	1925	29		42	4	
14-11-43		8,800	22	1936	32		30	7	85 lbs

TABLE 4

Case 13 S B<sub>1</sub> (30), Spleen not palpable Lymph nodes+ X ray shadows+

Date	Treatment	Total Leuco cytes	PERCENTAGE					
			Eosino phil %	Total Eosin	Neutro	Baso	Lympho	L M
20-1-44	Nab 0.15 gm	22,000	60	13,200	30	0	10	0
					0000		2200	
25-2-44								
26-1-44		21,000	60	12,600	30	0	10	0
2-2-44								
5-2-44		20,000	56	11,200	32	0	12	0
13-2-44								
20-2-44		12,000	45	5,400	35	0	20	0
29-2-44								
4-3-44		10,800	32	3,456	50	0	18	0
5-3-44								
11-3-44		9,800	16	1,568	49	0	35	0
12-3-44	NAB 0.60 gm							
17-3-44		9,000	69	810	59	0	32	0
					5310		2280	

TABLE 5

Case 31 V L T (28), Spleen not palpable Lymph nodes+, X ray shadows+

Date	Treatment	Total Leuco-cytes	Eosino-phils %	Total Eosin	N	B	L	LM	Weight
23-0-44		29 000	81	23,490	10	0	9	0	118 lbs
5-7-44	Carbarsone 0.25 g twice a day for 10 days	31,700	70	22,590	25	0	5	0	
7-7-44		10 500	81	8,225	41	0	10	1	122 lbs
17-7-44	Carbarsone 0.25 g twice a day for 10 days	9,600	12	1,176	60	0	27	1	128 lbs
14-8-44		7 400	12	888	72	0	16	0	144 lbs

TABLE 6

Case 40 S L M (40) Pern Anaemia, Spastic paraplegia (See fig 2B)

Date	Treatment	Total Leuco-cytes	Eosino-phils %	Total Eosin	N	B	L	LM
18-0-44		21,800	52	11 336	36	0	12	0
10-0-44 to 8-10-44	Carbarsone 0.25 g twice a day for 10 days							
29-0-44 to 8-10-44	No treatment							
9-10-44 to 18-10-44	Carbarsone 0.25 gm twice a day for 10 days	8,600	17	1,462	60	0	21	0
23-10-44		10,200	9	918	67	0	22	2

TABLE 7

Case 41 S (15) Lymph nodes+++ X Ray shadows+ (See Fig. 1)

Date	Treatment	Total Leuco-cytes	Eosino-phils %	Neutro	B	L	LM	ESR	Weight
1-10-44		34,000	63	28	0	18	1		75 lbs
8-10-44		33 000	73	10	0	12	2		
12-10-44		27 000	65	0	0	25	1	86mm	
16th to 26 10-44	Carbarsone 0.25 g BD for 10 days								
30-10-44		45,800	69	10	0	20	1	67mm	
1-11-44		35,000	60	11	0	29	0		
3-11-44 to 12-11-44	Carbarsone 0.25 g BD for 10 days								
10-11-44		22 000	42	21	0	84	3	25mm	84 lbs
20-11-44		16 500	30	24	0	38	2		
	Discharged symptom free								
	Returned again with symptoms								
17-2-45		28 100	67	11	0	26	2		
28-2-45		29 150	52		0	0	30		
3-3-45		16 000	40	25	0	35	0		85 lbs
	Penicillin 15 000 units Intramuscular 3 hourly, 7 000 000 units in 6 days from 4th to 9th								
4-3-45		21 000	68	18	0	15	2		
6-3-45		13,500	37	25	0	38	0	30mm	88 lbs
11-3-45		17 000	27	24	0	47	2		
13-3-45		14 000	30	23	0	45	0		
19-3-45		18 800	30	32	0	32	0		
	(1) Neocarsphenamine 0.15 gm with calcium & vitamin C								
21-3-45		12 500	22	38	0	38	2		
23-3-45		11,500	20	36	0	40	4		
	(2) Neocarsphenamine 0.3 gm with calcium & vitamin C								
25-3-45		12 000	25	36	0	35	4		
27-3-45		12 000	28	40	0	30	5		
	(3) Neocarsphenamine 0.45 g with calcium & vitamin C								
29-3-45		11,500	25	38	0	38	2		
31-3-45		10 500	24	33	0	42	1		
	(4) Neocarsphenamine 0.45 g with calcium & vitamin C								
8-4-45		1 0000	16	47	0	36	1		
5-4-45		10 000	14	46	0	40	1		
	(5) Neocarsphenamine 0.45 g calcium & vitamin C								
8-4-45		10 000	14	42	0	0	0		
	(6) Neocarsphenamine 0.45 g with calcium & Vitamin C								
13-4-45		8,000	18	35	52	0		5mm	88 lbs

## DISCUSSION PATHOGENESIS

During the years 1932-1936, Loeffler reported a clinical syndrome of eosinophilia with pulmonary shadows. His cases were afebrile and discovered in routine examination which included mass radiography. They had no or slight symptoms or physical signs. The blood eosinophilia ranged between 6 to 60 per cent. The x-ray shadows were of several forms: (1) large irregularly out-lined shadows which occupying a considerable portion of the lung field, (2) a small round shadow, (3) multiple small shadows in one or both lung fields, (4) foci sharply defined at the margins of the lobe, and (5) shadows in the vicinity of the hilum simulating hilar glandular enlargement. The shadows were fleeting and migratory, disappearing from 3 to 8 days and related to the blood eosinophilia, which sometimes persisted after the lungs had cleared. At first a tubercular pathology was

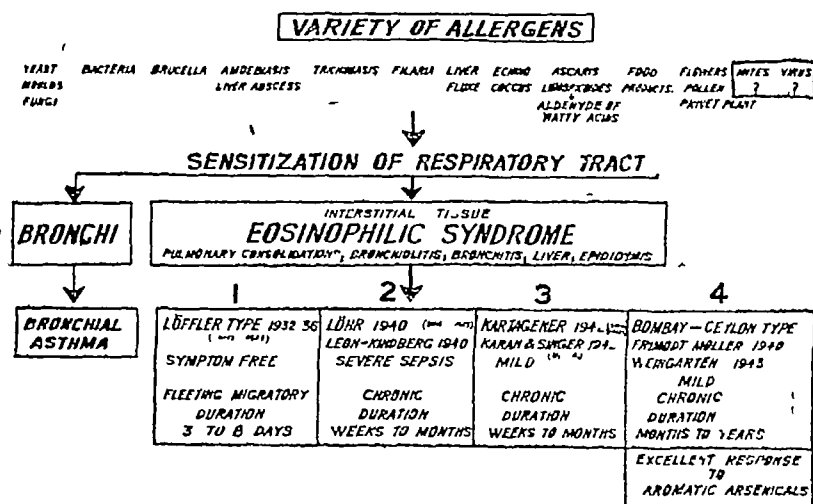


Fig 3 Showing the various types of Eosinophilic syndromes with pulmonary shadows. thought of in these cases, but in a review of 100 cases in Loeffler's clinic at Zurich, Maier found only 2 patients with active tuberculosis.

In 1940, Lohr and Leon-Kindberg independently described another type of pulmonary eosinophilic infiltrates which persisted for several months in patients who presented a rather septic clinical picture.

In 1942, Kartagener described a third type of pulmonary infiltration characterised by chronicity and mildness of clinical symptoms. Karan and Singer (1942) reported 5 cases from U.S.A. where the pulmonary shadows lasted from a few weeks to several months.

The pulmonary shadows seen in cases of benign eosinophilia in Bombay which run a prolonged course of several years duration, also, most probably, belong to the same category. It is probable that all these types are variants of an allergic syndrome produced by a multiplicity of causes. This view is illustrated in the scheme showed in fig. 3.

As to the nature of the pulmonary shadows, Hansen-Pruss and Goodman (1944) have suggested that they are really allergic pulmonary consolidations. There are no reports of the histopathological studies of the condition as it is a benign state, except that of Meyenburg (1942) who has reported autopsy findings in four patients, three of whom died immediately after injury, and one from fulminating tetanus. He found foci of pneumonia of varying form, extent and localization. They were found, wedge-shaped, or infarctoid. Microscopically all had in common a high grade eosinophilia in the inflammatory exudate. Other cellular elements were plasma cells, lymphocytes, alveolar cells and giant cells. Two cases showed eosinophilic bronchitis and bronchiolitis indicating the bronchopneumonic distribution of the lesions. Eosinophilic infiltration was also found in the liver and the epididymis in two cases. The infiltration in the alveoli and round about suggests that it is *the interstitial tissue of the lung that is hypersensitive and acts as a shock organ in the anaphylactic process, rather than the bronchi*, as in the case in bronchial asthma (Fig. 3).

As to the etiology of these allergic states, there is no agreement. Bacteria in the nasopharynx, *Ascaris lumbricoides*, flowering of the privet plant (Engel, Shanghai), and mites either *Tyroglyphus* or *Tarsonemus* (Carter, et al. Ceylon) have been variously suggested as probable allergens responsible for the eosinophilic syndrome. As mites are not susceptible to arsenic, they probably act as vectors of some virus. Viswanathan and Natarajan (1945) have observed 66 cases of tropical eosinophilia and have tested 105 sera for cold agglutination, of which 61 were from the cases of tropical eosinophilia. Of these, 53 gave positive cold agglutination, the titre varying from 1 in 16 to 1 in 2048, 27 giving high titre values above 1 in 256. Such high titre values were observed in atypical pneumonia of unknown etiology, probably virus. The condition is very frequent in Bombay and it is desirable to plan field studies and pathological investigations to elicit its etiology. It is essentially a benign condition and easily controlled by arsenic, and if mites are the vectors, it should not be difficult to produce the condition experimentally in volunteers. Manson-Bahr has found the eggs of mites in fresh faeces, but the eosinophils in these patients were under 10 per cent.

Weingarten does not accept the allergic interpretation of the syndrome. He considers the long and characteristic course of the disease, x-ray findings of the lungs, splenic enlargement, absence of skin or gastro-intestinal symptoms or signs, and the response to treatment, the constant and high leucocytosis with its remarkable eosinophilia, all points against allergy. In this connection it must be remembered that eosinophilia in blood or tissue is found frequently in scarlatina, and less frequently in varicella and variola, in other words, it is found in association with virus disease, and the possibility of virus etiology cannot be ruled out. The presence of eosinophilia in blood or tissue does not necessarily denote an allergic reaction. Our knowledge about



the exact function and significance of eosinophils in both blood and tissue, is indeed very meagre

In the bone marrow the eosinophils are derived from cells known as stem cells, lymphoidocytes, myeloblasts or haemocytoblasts. In addition to the formation of eosinophils in the bone marrow, tissue eosinophils are derived from various sources, such as lymphocytes, large mononuclear leucocytes, plasma cells and adventitial cells. The granules of eosinophils have a striking uniform diameter in contrast to the great variation in size of the granules of basophils. Originally the eosinophil granule was considered to be formed from the erythrocyte degeneration products. This view is now discarded and experimental studies have stressed the role played by protein sensitization in the origin of eosinophils. A single injection of suspensions of erythrocytes, haemoglobin, or egg albumin did not increase the number of eosinophils in leucocytes in the blood. However, repeated injections of these materials at intervals of eight to twelve days resulted in marked increase in eosinophil leucocytes in the blood stream and in the peritoneal cavity. Experimentally eosinophilia has been noted after injection of pilocarpine, inoculation with trichina, injection of extracts of *taenia solium*, or injection of aqueous extracts of *ascaris lumbricoides* (Stickney and Heck).

#### SUMMARY AND CONCLUSIONS

1 49 cases of massive eosinophilia seen in Bombay during the period from 1-10-43 to 30-11-44 (14 months) are analysed, the available literature on the subject is reviewed and its pathogenesis is discussed

2 The syndrome of massive eosinophilia, with cough, asthma-like attacks, loss of weight and pulmonary shadows is very common in Bombay. Many cases have enlarged glands. Splenic enlargement was rare in this series. The radiological changes could not be correlated with blood eosinophilia or with subjective symptoms.

3 Fever and splenic enlargement are more common in children. The occurrence of the syndrome in the presence of other diseases, congenital heart, mental disease, spinal paraplegia etc., is also noted.

4 The occurrence of this syndrome in *several members of one family* is reported.

5 The uniform response to aromatic arsenicals is noted, but the possibility of incomplete recovery is stressed if insufficient treatment is given.

6 During the course of treatment flare up of the subjective symptoms, high fever, and increase in the number of eosinophils, are noted.

7 Even with sufficient treatment, the occurrence of *relapses* is not uncommon.

8 The etiology of the syndrome is still obscure.

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## DISCUSSION

Dr R B Billimoria inquired about the source of eosinophilia and the reason why they increased in helminthiasis and allergic conditions. Eosinophilia was not always accompanied with complications in the lung. The eosinophilic granules might act as allergens producing asthma. He wanted to know whether acetylcholine had anything to do with eosinophilia. He observed a 5 to 10 per cent increase in eosinophils after injection of acetylcholine in cases of hypertension. He suggested a routine examination of stool in all cases of eosinophilia. He had also observed an increase of eosinophils in pulmonary tuberculosis and inquired whether arsenic could be given in such cases.

Dr V V Shah said, "I have seen ten cases of so-called tropical eosinophilia, four were private patients, four students of the National Medical College and two were from the out-patient department of the Bai Yamunabai Nair Charitable Hospital. The first case was seen by me in August 1943. He had paroxysmal attacks of cough mostly at night associated with a sense of suffocation, lassitude, anorexia, loss of weight and low fever in the early part of his illness. There were no signs in the chest except slight emphysema and harsh breath sounds. The total leucocytic count was 22,560 per cmm with 86 per cent eosinophils. A radiogram of the chest showed diffuse mottling, more marked at the bases and in the hilar regions. Other investigations, urine, stools and blood Kahn, were negative. He was treated with neoarsphenamine injections and was completely cured and to date there is no recurrence.

The diagnosis should not be based only on eosinophilia but the criteria should be the clinical picture, leucocytosis with eosinophilia and response to organic arsenicals. My impressions are that this

condition should not be mistaken with bronchial asthma. The patients, suffering from this syndrome, have to wake up at night and sit up in bed because of the severity of paroxysms of cough and a sense of suffocation but not because of attacks of dyspnoea. If dyspnoea is present, it is not a marked feature. In bronchial asthma, the patient complains of paroxysmal attacks of dyspnoea. Mine being a small number, it is very difficult for me to generalise a clinical picture, but from the close observation of my cases and as most of my cases were early cases (symptoms of less than fifteen days' duration), I should emphasize one point that in any future enquiry, the history taking should be thorough and the patients should be observed during the paroxysms. Apart from this there are other symptoms like lassitude, loss of weight, low fever, anorexia which make up the clinical picture. Even then, there may be borderline cases, which may be mistaken with bronchial asthma. In these cases, if there is leucocytosis with marked eosinophilia, a therapeutic trial to arsenicals should be given and if they respond, this should decide the diagnosis.

I may here mention a case of pulmonary tuberculosis (proved radiologically and by sputum examination) who after about two years, when the tubercular lesion was quiescent and healed, came to me for corza and paroxysmal attacks of cough especially at night and on examining the blood it showed a total W.B.C. 18,000 per cmm with 38 per cent eosinophils. The patient was treated with sulfarsenol injections and was completely relieved of the symptoms. It is, therefore, necessary to keep in mind that eosinophilia may be associated with or may follow pulmonary tuberculosis and it is worthwhile giving a therapeutic trial to arsenicals as this may help indirectly in preventing aggravation of a tubercular lesion already existing or in not allowing the old tubercular lesion to flare up."

**Dr S G Joshi** agreed with the speaker that the cases observed by him began with rhinitis. He was of the opinion that they were vasomotor in origin. He divided them into three types: the first purely a rhinitis, the second in which the lung showed signs of bronchial asthma in addition to the affection in the nose and in the third type the nasal condition disappeared and the bronchial asthma persisted. In the cases with rhinitis he had found ionisation with zinc a useful procedure.

**Dr S K Vaidya** made some observations on eosinophilia. He deplored the tendency to give new names to diseases and mentioned that conditions like sprue, epidemic encephalitis which were obsessions at one time, had now lost the importance that was given to them. He then continued "I have here 42 cases of eosinophilic blood-pictures collected from my laboratory records dating from October 1943 to first week of March 1945, a period of 17 months, the total leucocytes ranging from 6,400 to 41,000 and total eosinophils ranging from 750 to 32,600 per cmm the relative percentage varying from 10 to 81.5, to show that the syndrome of eosinophilia is not a rare one, nor is so-called "Tropical eosinophilia" likely to turn out to be a new disease, but it is more

likely to be ultimately grouped as an eosinophilic-symptom-complex due to various allergens. Instead of going into the details of these cases most of which tally practically in all details with those described by Dr Patel in his very interesting paper tonight, I would like to show the really causative effect of Familial-genetic-inherited-cellular-tendencies, by describing my cases No 23 and 41, where family history of "asthma"-allergens is obtainable.

No 23, a young lad of 16 years, my great nephew, was going downhill in health due to troublesome cough. His father is well and free from cough. But his grandfather was a confirmed subject for asthma during the last 15 years and his great-grandfather also was an asthma subject and had in those old days to take recourse to the habit of opium taking for the complaint. Here his father escapes. But his mother had a grandmother in her father's side who was a confirmed asthmatic and had also to take opium, now and then, till she died of very old age. This shows that the eosinophilic-tendency genes inherited by his father being weak could not give asthma to him but when the son was reproduced by association with the eosinophilic tendency-genes contributed by his mother, they reinforced the tendency and gave him very pronounced "asthma-like" cough and pronounced eosinophilia of 32,600 in a total leucocyte count of 40,000 per cmm, with a relative 81.50 per cent eosinophil count. And the most interesting thing is that one 0.3 gm neoarsphenamine injection set him right, with practically complete relief from troublesome cough and with good restored sleep and rest at night since the very second night after the injection. Only one complication arose. He had dermatitis all over the body and diarrhoea for 2 days, but he made a good recovery and when his blood was examined six weeks later, he showed only 8000 total leucocytes with 1120 eosinophils per cmm and 14 per cent relative eosinophil count. He is now taking arsenic by mouth.

Similar is the family history of my case No 41. He is now 62 years old, he has been getting typical attacks of asthma, and is now an established chronic case with bronchitis and emphysema. His eosinophil counts have been often done and they keep on changing the highest relative count being well over 60 per cent the lowest being 5 per cent and only a fortnight back his counts were total leucocytes 10,000 total eosinophils, 1275 per cmm with 12.75 per cent relative eosinophil count. He has had a large number of arsenical injections which gave him relief for a time. But of late there is a tendency to more frequent relapses with return of eosinophilia. He gets temporary immediate relief by adrenalin by injection and also some benefit by ephedrine, which unfortunately gives him headaches. The last count was done after three arsenical injections within two months. His father had only some cough after he was 60 years of age but no typical asthma, while his grandfather had very bad asthma and had to take opium for relief. In the parallel branch of cousins, his two great-uncles had asthma and some of their children also have asthma and

their children, chiefly males, show marked eosinophilia with asthmatic attacks, before they have reached their thirtieth and even twentieth year of age. His son, aged 12, has cough and eosinophilia 2880 per cmm (36 per cent)

I know these cases well and the family history also indubitably well, because they are all very closely related to me and also many of them come from families whose profession was that of Ayurvedic physicians, and whose business it was to make a study of medicine as a speciality. From the follow up and the family history of these two cases, it seems that relapses are frequent and common. Some of these cases, progress to a condition of chronic bronchitis and asthma.

I must thus utter a warning against being carried away by obsession of considering eosinophilia as something new in the line of diseases. I feel certain that after a time fashions will change and the medical science will reassess the valuation of this symptom-complex."

**Dr P Raghavan** said, "I should like to cite a few cases which illustrate the clinical and other features of this syndrome. Of these one was a doctor who was under close observation. The condition started with low fever and paroxysmal attacks cough and breathlessness at night. There was a leucocytosis of 41,000 per cmm with 75 per cent eosinophils. The stools showed nothing abnormal and the radiogram showed increased lung markings and infiltration at both bases (see fig 3 on plate facing page 98). The nocturnal cough and dyspnoea were relieved with injections of adrenalin and then he was given carbarsone 0.25 g twice daily. At the end of the course of carbarsone the patient had been relieved of his symptoms, felt much better and the leucocytic count had come down to 14,050 per cmm with 22 per cent eosinophils. A second radiogram (see fig 4 on plate facing page 98) taken at this stage showed clearance of shadows. Since the count had not come down to normal he was subsequently given a course of intravenous neoarsphenamine. He is completely free from symptoms for the last 2 months. The other case was that of a foreman in a leather-trade school whose trouble started few days after a rat-bite two years prior to his coming under observation. He had no fever or rash at any time but a paroxysmal cough with a sensation of choking mostly at night. He had a leucocytic count of 17,000 per cmm with 42 per cent eosinophils. His symptoms cleared with intravenous neoarsphenamine."

Though the cough which is characteristic has been emphasised it is not cough alone, but the dyspnoea and the choking sensation as well that disturbs the patient. There is another feature which has not been emphasised and that is the relief which adrenalin gives to these patients. In spite of these points of similarity to bronchial asthma it seems justifiable to differentiate it as a separate clinical entity because of the leucocytosis and associated eosinophilia, the peculiar radiographic picture, and the clearance of the symptoms and the return to normal of the haematologic and radiographic abnormalities.

on the administration of intravenous or oral arsenic. Whether it will survive as a distinct aetiological entity is a question which only further investigations can decide."

Dr J C Patel said that he did not want to enumerate the straightforward cases of eosinophilia which were seen by him in his practice but he would like to mention three cases in which eosinophilia was present on blood examination and M tuberculosis was detected in the sputum. The total eosinophils were (1) 5,160, (2) 1,400, and (3) 1000 per cmm. The stool was examined in two of them, in one case roundworm ova were found. He suggested that in cases of paroxysmal cough which were being investigated for tropical eosinophilia a routine examination of the stool may be done in addition to a blood count and radiographic examination of the chest. He added that eosinophils had a high histamine content and shadows in the lung may be due to exudation in lung tissue just as urticarial wheal occurs in skin and because of that, shadows in lungs may appear and disappear quickly which has been the observations of Loeffler, known as "Loeffler's syndrome". He also inquired whether arsenic given in cases described above would do any harm to the individual. He also made an observation that many immature eosinophils were seen in these cases.

Dr R G Dhayagude remarked that Dr Patel had included in his collection cases in which x-ray examination was not made. He felt that besides the clinical features of the case an x-ray evidence of mottling and eosinophilic blood picture should be included as criteria when different cases worked out by several workers were to be compared. He said that he was aware of the work of the Ceylon workers who had incriminated some type of mite as the cause of eosinophilic lung. Dr Monteiro in his department investigated a few cases on a request from Dr J C Patel, in order to detect the presence of mites. The results were not successful. The problem as regards the etiology of this interesting condition needed further work and he would be glad to participate in any scheme of investigation undertaken with this end in view.

Dr N D Patel, replying to the points raised during the discussion, observed that (1) though there was much experimental work about the production and function of eosinophils in health and in disease, there was no final agreement, and there was still much scope for further experimental research. (2) Whether eosinophilia found in cases of tuberculosis was due to tubercular infection or was an associated superimposed malady, there could be no objection to its being treated with arsenic, if only it relieved the patient of harassing cough and nocturnal asthma-like attacks. (3) Considering the frequency of round-worm infestation, the occasional finding of the ova in the stool of a patient with eosinophilia can have little etiological significance. (4) Though harassing cough was the prominent feature of the syndrome many patients had breathlessness also, and some even severe enough to merit the name status asthmaticus. The response

to adrenaline or ephedrine was always satisfactory as regards symptomatic relief (5) Many cases of Familial or Constitutional Eosinophilia are recorded in the literature but at this stage it appears best to keep cases of Benign Eosinophilia which react so favourably to arsenic apart by themselves till further evidence is produced to link them up with cases of familial or constitutional eosinophilia Also, it is best not to mix them up with cases of Eosinophilic Leukaemia

**Dr V R Khanolkar**, in summing up the discussion said that with regard to the histological findings in the lymph nodes supplied by Dr Patel from cases of eosinophilia the work was still incomplete and hence no conclusions could be drawn at this stage He mentioned that the symmetrical enlargement of lymph nodes occurring in well-fed children disappeared after a time but at some later date in some cases developed into lymphosarcoma He suggested that the study of lymph nodes should be continued as further light might be thrown on this syndrome

Dr Khanolkar saw no objection in separating out a distinct clinical entity from the vast subject of bronchial asthma, if the facts permitted In his opinion, it was only by such limitation of the field of inquiry that progress in medicine was possible

(Continued from p 120)

## MALARIA

### 38

Except in cases of malignant tertian, treatment, when possible, should, particularly with benign tertian and quartan fevers, be commenced only after several attacks, when co-operation of the body's natural powers of resistance may be looked for

### 39

In cases of quinine idiosyncrasy or acquired quinine hypersensitivity, quinidine or hydroquinidine may be used without ill-effects

### 40

With adequate quinine therapy the temperature should definitely return to normal not later than the sixth day and remain so for a fairly long time even should treatment be temporarily stopped There should also be no small sub-febrile increases of temperature If the temperature rises again during quinine, or in the intervals of this, even if only to small subfebrile heights, we are confronted either with an incorrect diagnosis, or a complication, or a faulty preparation, or with loss of quinine efficacy due to too long use of the drug An acquired hypersensitivity to quinine can also cause such a 'pseudo-relapse' or 'paradoxical quinine fever'

# Reflections & Aphorisms

## MALARIA

1

To understand the clinical picture of malaria one must realize that it is a chronic disease, as are most protozoan blood infections. For fever-attacks are merely symptoms of temporary increase in the number of parasites present in the blood, as the malaria process does not entirely cease between attacks.

2

If there is no further infection, malaria definitely cures itself after some years, and in course of time its after-effects disappear. Malignant tertian undergoes spontaneous cure most quickly, usually in from one to two years, benign tertian in from four to five years, but quartan malaria may continue longer, but only exceptionally.

3

The incubation period of malaria is 10 to 14 days but in persons who had prophylactic quinine the infection may remain latent and the incubation period may last several months, a year or even longer.

4

Extended latency of tertian malaria in temperate zones is generally recognised. Infection in summer or in autumn is generally followed by an acute attack next spring or even summer.

5

Small unnoticed attacks, shivering without reason, sense of heat, and occasionally catarrhal or "gastric" fever make up "abortive malarias" which are quite common, especially in the case of patients who have undergone prophylactic treatment.

6

The prodromal symptoms of malaria nearly always appear, and the individuals who have had frequent attacks recognize that their 'fever' is returning, when they feel tiredness, pain in the bones and limbs, lack of appetite, occasionally pain over spleen, and initial fever, a slight continuous rise in temperature.

7

A correct picture of the course of the fever in malaria attacks is only obtainable by taking the temperature at least six or eight times during every 24 hours, and the night temperature must be taken as well, not for routine clinical work, but if a reliable curve is required for diagnostic or scientific purposes, this method is essential to avoid errors.



## 8

The curve of malignant tertian is obviously of tertian type, but each attack lasts longer, from sixteen to eighteen hours and more, so that the end and the beginning of two consecutive attacks may occur on a day when fever should be absent. The temperature does not rise so suddenly as in tertian and quartan. The shivering fit, therefore, is often absent, or only very slight. The fever stage is considerably extended, and at its climax quotidian. The fever decline follows, and this also may often be interrupted by one or several sharp peaks.

## 9

Other than shivering fits, fever, and perspiration, the associated symptoms of malarial attack are headache, rapid pulse, complete lack of appetite, exhausting vomiting, at times even bilious (biliary fever), hiccup, severe and lasting for days, and pains in the spleen. Catarrhal symptoms such as coryza, cough or diarrhoea are not uncommon.

## 10

The pains in the spleen are very characteristic. They radiate throughout the surrounding organs and may, under certain conditions, simulate pleural or pneumonic affections.

## 11

The splenic enlargement which develops in the course of malaria is at first soft, scarcely palpable, and often only demonstrable by percussion. In some rare cases rupture of spleen occurs, leading to hæmorrhage and to death unless immediate operation is performed. The rupture is usually caused by trauma such as a fall or a blow, but it may be spontaneous for instance, after violent vomiting. Sudden apparently peritoneal symptoms give indications. The hard and easily palpable, often very large, swelling of the spleen develops only gradually in the course of longer infections.

## 12

A not infrequent concomitant of benign tertian malaria, much more rarely of quartan or malignant tertian, is herpes affecting the lips, mouth or face, and frequently the ear. True herpes zoster can also appear with malaria, also it may appear as a sequel of malaria or in masked forms of malaria.

## 13

Malarial fever is often associated with an acute erythema. Skin exanthemata, roseola, purpura and petechial hæmorrhages, may occur in malaria, though infrequent.

## 14

The presence of mature form of malignant tertian parasites especially of schizonts, in the peripheral blood stream must always be taken as a grave sign. Often it is a preliminary warning that cerebral malaria is threatening.

## 15

In Algid or Cardiac form of malaria, there are rapid loss of strength, extreme cardiac weakness, hippocratic facies, threatening collapse, intense perspiration, and cold skin, low axillary temperature but high rectal reading

## 16

In comatose forms of malaria, the patients are usually apathetic from the very beginning, even before the onset of the attack. The apathy increases during the attack itself, passing into stupor and coma. In some cases this condition occurs in the course of a bout of a fever which at first seems quite mild, or after several preceding attacks of a comparatively mild nature. The temperature is not always very high. With few exceptions the comatose form occurs only in malignant tertian infection in first attacks as well as in relapses

## 17

Bleeding from the skin, mouth, nose, stomach, intestines, lungs, female sexual organs, or eyes appears as a direct effect of severe malignant tertian infection, although not often. It responds well to quinine therapy, haemorrhages due to quinine idiosyncrasy are made worse

## 18

Apart from the severe dysenteric forms of malignant tertian, milder dysenteric or diarrhoeic conditions occur particularly in cases of primary fever. It should be emphasised that in many cases the symptoms are very similar to those in appendicitis

## 19

Glycosuria has occasionally been observed in malaria, and its direct connection with malaria was deduced from its disappearance after intensive quinine therapy

## 20

Slight albuminuria occurs in some cases in the initial stage, its occurrence during the course of quinine medication may be a sign of an impending attack of blackwater fever

## 21

Nephrosis and nephritis frequently complicate quartan malaria, generalised anasarca sometimes responds favourably to quinine therapy. Oedema without albuminuria has been reported in quartan fever.

## 22

Malarial amblyopia is usually transient, and is differentiated from quinine amaurosis by haemorrhages of the blood vessels and dark bloodshot flecks around the macula. Severe, even fatal haemorrhages after quinine have been observed. Visual disturbances after quinine

are rare, occur quite suddenly, affect both eyes, produce at first diminution of the field of vision and are often accompanied by disturbances of hearing. The visual disturbances occurring as a sequel to malaria develop only in malarial cachexia when too little quinine rather than too much has been given. The visual disturbance gradually increases, but it does not necessarily affect both eyes, neither is it combined with deafness, nor does it usually lead to complete loss of sight. The prognosis is favourable if it is possible to give a thorough treatment of malaria with all possible precautions. The prognosis is unfavourable in quinine amaurosis, as almost invariably atrophy of the optic nerve subsequently develops.

## 23

Children are particularly susceptible to malaria. It is characteristic that both shivering and sweating may be entirely absent, as also any marked rise in temperature, the fever often occurring at night and thus escaping notice. The children are lethargic, querulous, and apathetic with a grey unhealthy look, thoroughly run down and anaemic, with a considerable splenic enlargement. Convulsions are a characteristic symptom of malarial infection in children. Spasms in babies and young children are very often thus caused and take the form of clonic or tonic contractions, though they may also be of an epileptic type.

## 24

The auto-immunization in malaria is not complete, and sooner or later relapses occur. Spontaneous remission usually occurs only after frequent relapses. The spleen probably plays an important part in the process of incomplete immunization, which leads to the temporary disappearance of the attacks when treatment is either insufficient or entirely absent. Absence or extirpation of spleen results in acute pyrexial attacks with a great increase of parasites and a certain fatal course, resisting every form of quinine therapy.

## 25

Relapses are observed in regular sequences, e.g., after seven days, but mostly after three weeks. Relapses are frequently brought about by changes in climate, shocks to the system, such as cold, wetting during marches, muscular exertion, by injuries, childbirth, surgical interferences, exposure to intense sunshine, by errors of diet, alcoholic excesses, mental excitement, sexual excesses, and strong purgatives, by any kind of preventive inoculation, e.g., against typhoid, cholera, smallpox, etc., by injections of sterile milk, serum, or salvarsan, or during the prodromal and early stage of acute infectious diseases, such as enteric fevers or influenza.

## 26

Relapses are due to what is described as "labile infection", or 'dumb infection', or 'premunitio'. The asexual development of the

parasites is inhibited through the action of the protective bodies of the organism. These undeveloped young parasites are present in the reticulo-endothelium system, are viable and reproduce themselves as a result of some occasional disturbance, and a relapse is brought about. Schaudinn's 'regressive schizogony of the merozoogametes' though confirmed by many, is not considered nowadays to be proved.

### 27

The first relapse is usually rudimentary, but in malignant tertian the second or the third relapse may well be pernicious. Relapse follows a latent stage, and relapses and latent periods may alternate over a long period.

### 28

In malarial cachexia, it is sometimes possible to observe schizogony in the peripheral blood-stream, although the usual paroxysm may be absent.

### 29

Masked malaria usually takes the form of neuralgia, particularly of the trigeminal type. These attacks sometimes recur regularly, but disappear only to return later. 'Subclinical malaria' is seen in ambulant persons. The chief complaints are recurrent headaches, backache, aching limbs and malaise. 'Latent malaria' means a symptomless parasitization.

### 30

Malaria and acute infectious fevers show a certain mutual antagonism in so far as acute malaria attacks are clinically masked during the febrile stage of the disease. Such malaria attacks can only be positively diagnosed in the incubation period or prodromal stage and again after the acute symptoms have subsided.

### 31

Leucopenia and monocytosis in the white blood cells and basophilia and polychromasia of the red blood cells are characteristic of malaria. Pronounced leucocytosis, especially if found repeatedly, contraindicates the presence of malaria.

### 32

Whenever malaria is suspected several thick film preparations should be examined for the presence of parasites by an experienced worker, and a routine blood count with total and differential white count must be obtained. The absence of parasites does not rule out the presence of malaria, conversely, the presence of gametocytes alone does not justify the assumption that the particular fever is malaria. It can just as well be a feverish disease superimposed on a chronic latent malarial infection.

## 33

The diagnosis of malaria should be made on (a) typical history and constitutional and local symptoms (b) temperature curve, (c) presence of urobilin and urobilinogen in urine during an attack and for some days after, (d) typical blood findings, (e) Henry's reaction, and (f) effect of quinine or atebirin

## 34

When, in the case of a acute feverish disease, atebirin or quinine, —supposing that either has been correctly administered in sufficient amounts,—does not succeed after three or five days in reducing the temperature to normal for at least a few days, so that there are not even small fever peaks to be observed, then it is not malaria

## 35

In the differential diagnosis of malaria, apart from enteric fevers and intermittent malaria-like fevers caused by a variety of different conditions, relatively rare diseases such as (a) haemolytic acholuric jaundice, (b) aleukaemic leukaemia, (c) relapsing fevers, and (d) early stages of kala-azar should be considered

## 36

Quinine treatment of malaria is no *therapia magna sterillans*. However large and however frequent the doses, relapses are inevitable. The malaria parasites are not influenced to the same extent at their various stages of development. The youngest forms are the most susceptible and the gametocytes have the strongest power of resistance.

When quinine is given continuously in daily doses over a long period the therapeutic action becomes progressively less pronounced. At the same time the patient may develop a hypersensitiveness to the drug which expresses itself in the appearance of unusual secondary effects, such as otherwise observed only in cases of quinine idiosyncrasy.

## 37

Excessive doses of quinine as a rule have no advantage over moderate doses. To be effective quinine must be present in the body in sufficient quantity at the time when the youngest parasites make their appearance and are most abundant, i.e., at the beginning of an attack, before and during the shivering stage, and immediately afterwards. This can best be achieved by giving small doses at regularly spaced intervals, irrespective of the state of the patient. Relapses cannot be prevented by quinine and occur in at least 25 to 50 per cent of cases in spite of the administration of maximum doses of quinine for as long a time as possible. An average of 15 grains (3 doses of 5 grains each or 5 doses of 3 grains each) of quinine hydrochloride should be given to adults as long as there is fever and for five days after the temperature has dropped to normal (i.e. for 7 to 10 days in all) and this short treatment should be repeated during relapses as often as they occur.

(Continued on p 114)



The diagnosis in the four cases that recovered was not considered by Mehta to be beyond doubt as the pneumococcus had not been grown in culture of the cerebro-spinal fluid in any of these cases before treatment. Thus even with sulphapyridine and sulphadiazine the mortality rate comes to 100 per cent.

In the last year reports have appeared of recovery of cases from pneumococcal meningitis on treatment with penicillin alone<sup>4,5</sup> or penicillin combined with sulphonamides<sup>6</sup>. Dawson and Hobby<sup>4</sup> reported four consecutive recoveries, with a dosage ranging from 440,000 to 975,000 units of penicillin. Cairns and his co-workers<sup>5</sup> had twelve recoveries in sixteen consecutive cases. Waring and Smith<sup>6</sup> had eleven recoveries in twelve consecutive cases treated with combined penicillin and sulphonamides. Bloomfield<sup>7</sup> however did not have such a sanguine experience as even the cases that recovered had crippling neuro-psychiatric sequels. He considered as probable causes for the failure to be too brief a duration of treatment, too small a dosage, lack of combined surgical drainage, the presence of overwhelming infection, and, or the presence of a complication like nephritis which is not influenced by penicillin.

Since our experience with sulphonamides in pneumococcal meningitis has not been satisfactory it was considered worth while to report the following two cases which responded to treatment with penicillin.

**Case 1** (R 15701) S K, female aged 35 was admitted in a semi-comatose state with intermittent episodes of delirium. The relatives gave a history of continuous fever and a headache of four days' duration. On admission temperature was 102°F, pulse was 114 and respirations were 30. No abnormal physical signs could be detected in the cardio-respiratory system. She had marked neck rigidity and bilaterally positive Kernig's sign and Babinski's response. The ears were healthy and no induration could be seen on the mastoid region. The cerebro-spinal fluid drained by lumbar puncture was under tension and turbid yellowish in colour and showed increased proteins with 3,172 cells per cmm, with a predominance of poly-morpho-nuclear-cells. Pneumococci were seen in smears and were grown subsequently in culture. The patient was given 4 grams of sulphamerazine immediately by a stomach tube and 2 grams subsequently every four hours. Twenty-four hours later it was noticed that the patient had developed left sided abducens nerve paralysis. In spite of continuing sulphamerazine in full doses the patient was still semi-conscious at the end of forty-eight hours and had developed infra-nuclear facial paralysis on the right side. The spinal fluid showed less turbidity, 1,440 cells, and though no organisms could be seen in smears the pneumococcus could be grown in culture. In view of the absence of improvement in the clinical condition of the patient, sulphamerazine was stopped and the patient was given 10,000 units of sodium penicillin intrathecally which was repeated every twelve hours, and after an initial dose of 20,000 units intravenously she was given 10,000 units intramuscularly every 4 hours. Twelve hours after the first dose of penicillin was given the patient regained consciousness and was more

co-operative From then on she improved gradually and the temperature settled down to normal on the 3rd day after the beginning of the administration of penicillin The cerebro-spinal fluid was clear and sterile on examination She had a total dosage of 230,000 units of penicillin The facial paralysis persisted In view of this the middle ear and sinuses were examined for evidence of infection of which none could be found The patient was discharged from the hospital four weeks after admission in a normal condition except for the residual facial palsy She could not be traced later as she had left for a holiday to Goa soon after she was discharged from the hospital

*Case 2* (R 16554) G B, female aged 18 years, was admitted in a semi-conscious condition with a history of fever and pain in arms and legs of one day's duration On admission it was found she had inter-ludes of violent delirium alternating with periods of semi-consciousness No abnormal physical signs except neck rigidity, positive Kering's, and bilaterally positive Babinski's response, were elicited The cerebro-spinal fluid was turbid and showed 4,400 cells per cmm with 75 per cent of polymorpho-nuclear cells No organisms could be seen in smears but pneumococcus was grown in culture The patient was given 1 gram of sodium sulphapyridine intramuscularly and 4 grams by a stomach tube, followed by 3 grams every four hours After a few hours she developed vomiting Sulphamerazine was substituted for sulphapyridine On the second day after admission the vomiting persisted and the patient was still very irritable and unco-operative Sulphamerazine was stopped and 20,000 units of sodium penicillin was given intrathecally and was repeated in doses of 15,000 units every twelve hours At the same time after an initial dose of 20,000 units intravenously, 15,000 units were given intra-muscularly every four hours Seventeen hours after the first dose of penicillin had been given the patient regained consciousness Then she improved slowly She was given a total dose of 375,000 units of sodium penicillin During convalescence the temperature showed an irregular rise upto 99.5°F for which no cause could be found She was kept in the hospital for two weeks after the temperature had touched normal and was discharged as she was able to walk about and attend to herself without discomfort She was admitted again two months later for inability to walk and pain in the lower lumbar region of the spine which had developed about two weeks after she had left the hospital No abnormal physical signs could be elicited except rigidity of the right erector spinae muscles and an area of tenderness on deep pressure over the muscle at the level of the 4th lumbar vertebra She could be made to walk gradually with suggestion and persuasion, and the rigidity disappeared eventually with local infiltration of 1 per cent novocain solution The cerebro-spinal fluid examined during the second admission was normal, on cytological and bacteriological examination

#### COMMENT

In both these cases no evidence of pneumococcal infection could be found elsewhere in the body In both, the initial response to sulphonamide therapy was not satisfactory in spite of fairly massive doses,



In one of them the sulphonamide compound had to be stopped because of persistent vomiting. Within a short time of administration of penicillin there was clinical improvement. The total doses of penicillin given (230,000 and 375,000 units) was small and still recovery ensued. Perhaps it may be explained by the fact that both these patients had sulphonamides prior to their being given penicillin. One of them had a residual facial palsy for which no cause could be found in the middle ear or mastoid cells and the other developed later a functional paraplegia which eventually cleared up. Penicillin alone or in combination with sulphonamides offers a good prospect of recovery in cases of pneumococcal meningitis, but it has to be appreciated that the treatment must be local as well as general and it must be used intramuscularly or intravenously as well as intrathecally. Perhaps the intrathecal administration of penicillin may be given up in future, because penicillin is excreted in sufficient concentration in cerebro-spinal fluid after systemic administration.

#### SUMMARY

- 1 A brief review of the pertinent literature on pneumococcal meningitis is given
- 2 Two cases of pneumococcal meningitis which recovered on treatment with penicillin are reported

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#### DISCUSSION

Dr N K Sahar said that these were the first two cases of pneumococcal meningitis which were successfully treated in this institution. He related his personal experience in the treatment of 4 cases of pneumococcal meningitis with large doses of sulfonamides without any success. He mentioned one case in which the meningitis had developed following lobar pneumonia which was diagnosed at a very early stage when the cell count in C.S.F. was 630 per c mm. This patient was treated with 200 gms, of sulphapyridine in 5 days the drug being administered by all routes. The criteria for diagnosis of pneumococcal meningitis and its complete cure must finally rest with the result of a cultural examination of C.S.F.

Dr A Hameed related his experience in treating cases of pneumococcal meningitis. He mentioned two cases treated with penicillin unsuccessfully.

Dr N D. Patel remarked that from recent experimental work it is known that when penicillin is given by intramuscular or intravenous route the concentration of penicillin in C.S.F. was sufficient enough to act on the micro-organisms. Besides this in pneumococcal menin-

gitis there was a septicaemia and treatment by intramuscular or intravenous route was necessary

Dr R. G Dhayagude agreed with Dr Sahlar that cultural examination was the one to be relied on the diagnosis. He explained the difficulty of reporting on a smear examination alone especially in fluids which are not seen soon after removal. The staining and morphological characters change considerably with the increase of interval between lumbar puncture and the examination

Dr A. V Balga suggested that the rigidity of the back muscle of the second patient should be investigated and a general anaesthetic might exclude a functional cause.

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## DISORDERS OF THE GALL BLADDER\*

### OBSERVATIONS ON THE UNUSUAL ETIOLOGICAL FACTORS

by

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The usual type of pathological gall bladder that is found by surgeons is inflammatory in nature either with or without stones. But there are some rare cases where the patient has the symptoms suggesting disease of the gall bladder of an inflammatory nature but on opening up the abdomen the gall bladder is found to be not much inflamed but possessing some sort of abnormality, congenital or otherwise, either in the organ itself or in the structures closely related to it, anatomically and physiologically.

In the series of about 112 cholecystectomies done by me for various pathological conditions of the gall bladder, the majority had some sort of inflammation subacute or chronic with the concomittant changes in the allied structures such as dilatation of the common bile duct, adhesions to the surrounding structures, presence of enlarged lymph glands at the junction of the cystic duct and common bile duct.

But in about eight cases some abnormalities were found either in the blood supply of the gall bladder, the position of the gall bladder or in the size of the lumen of the biliary ducts.

In a case where the patient had all the symptoms of gall bladder trouble, the organ was found to be grossly pathological due to an abnormal branch of the hepatic artery passing the walls of the gall bladder before it entered the right lobe of the liver.

In another case the gall bladder symptoms were found to be due to a small papilloma lying on the outer surface of the fundus. In two cases of symptoms of pain, distension and dyspepsia were found to be due to a very narrow lumen of the cystic duct and the common bile duct. The removal of the gall bladder which was slightly patholo-

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\*A paper read at the 47th Scientific Meeting of the G. S. Medical College and the K. E. M. Hospital Staff Society, Bombay, on April 14, 1945, with Dr T. O. Shah F.R.C.S. (Eng.), in the Chair.

gical, cured the symptoms most probably as a result of the dilatation of lumen of the common bile duct which follows cholecystectomy

In two cases the gall bladder was found lying obliquely parallel to the anterior of the liver with the fundal wall buried in the substance of the liver to about one-third of its circumference

Skiagram does not always reveal the pathological condition of the gall bladder In one case with chronic cholecystitis of about twelve years' duration the radiological picture with the dye was that of normally filling gall bladder, although the gall bladder was pathological containing about seven fairly big stones of the mixed variety

Some cases have been found where the pain in the pathological conditions of the gall bladder is present, more on the left side of the abdomen, although local tenderness is present in the right hypochondrium

One comes across a fairly large number of cases who complain of pain in the cardiac area and are diagnosed as angina or pseudo-angina

In good many of these cases, especially in the early mild cases it has been found that the primary trouble is in the gall bladder and the pain due to chronic cholecystitis is referred to the cardiac area In such cases the heart is found to be quite normal

In long-standing cases of cholecystitis the heart muscle is found to undergo degeneration and the arteries tend to become atheromatous Thus in the long run a condition of regular angina pectoris may develop Cases have been quoted where removal of the gall bladder has stopped the so-called attacks of angina pectoris

As regards the treatment of cholecystitis medical treatment should be tried for some time before cholecystectomy is done There colicky pain occurring at long intervals is not necessarily an indication for operation especially in educated well-to-do patients Regular habits combined with drugs containing bile salts have been found to give good deal of relief in such patients But patients with persistent gall bladder symptoms like dyspepsia, general ill health with local symptoms like pain, and tenderness should have their gall bladder removed An acute attack of cholecystitis with fever, pain and jaundice is an indication for operation which should be done during the quiescent stage On opening the abdomen the indications for cholecystectomy are a gall bladder with its coat fibrosed or friable, a greatly dilated common bile duct, presence of Lund's sentinel glands at the junction of the cystic duct and common bile duct and adhesions round about the viscus especially near the cystic duct

All the same more importance should be given to the clinical symptoms especially their long duration, persistent character and their adverse effect on the general health when operative treatment is seriously thought of

Pain after removal of the gall bladder is common in the majority of cases But it usually disappears after almost two to three months In some cases of advanced gall bladder disease urinary symptoms like haematuria may be present which occurred in one of

my cases Radiological examination revealed no lesion of the urinary system Most probably the presence of jaundice in such cases gives rise to a tendency to bleeding which is the cause of haematuria It is of comparatively rare occurrence and disappears after treatment of the gall bladder condition

#### DISCUSSION

Dr S B Gadgil said that it was exactly two centuries ago (1745) that the first operation on the gall bladder was done In his opinion concentration of the bile gave rise to symptoms The curettage of the mucous membrane and cauterization would probably give the same results as removal of the gall bladder He further stated that a large number of abnormal gall bladders were found at the autopsy and in these cases no symptoms were observed during life A follow-up of the operated cases was necessary for the proper evaluation of results

Dr N D Patel speaking about the relation of gall bladder disease to angina pectoris said that the basis was probably a disturbance in the metabolism of cholesterol

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## ACUTE PARANITRANILINE POISONING

### A REPORT OF FOUR CASES

by

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On the evening of the 22nd of June 1944, B.A., and B.M., two Hindu males, aged about 35 years, coolies by occupation, were employed by an individual to transport a cask, on a hand cart, containing a yellow powder from Dadar to Kalbadevi, a distance of about 8 miles They reached their destination at about 10-30 p.m., delivered their goods, and started on their return journey, when one of them (B.M.) felt very exhausted and complained of giddiness and nausea The other (B.A.) put him on the cart, on which was lying some of the yellow powder which they had just transported, and pushed him back half the way to their destination, when he himself felt very weak and found it impossible to push the cart any farther Both of them lay down to sleep on the pavement At about 8-00 a.m., the next morning, they were picked up in an unconscious condition from the pavement by a policeman and brought to the K. E. M. Hospital

Case 1—B.M., when examined, was in a state of semi-consciousness, and could be roused with difficulty from his stupor He, however, was able to give a history of a feeling of feverishness and severe pain in the abdomen and vomiting of 8 hours' duration and not having passed any urine for the last 12 hours His temperature was 97°F, pulse

rate 140 per minute, respiration 40 per minute. The pupils and conjunctivae were normal, the tongue was dry and covered with a fur, and showed no cyanosis. There was a marked rigidity of the abdominal wall in the upper segments with absence of abdominal reflexes in those segments. Rectal examination did not show any tenderness in the Douglas's pouch. No other abnormality was detected. In the absence of a detailed history, a diagnosis of an acute abdominal catastrophe was made, but the patient refused to undergo any operative interference and was consequently kept under observation. Within 2 hours of admission he developed a yellowish pigmentation of the skin of the soles and the palms which gradually spread to the other parts of the body, and his tongue showed a peculiar leaden hue. He became cold and clammy and died within 5 hours of admission. An autopsy was performed which showed congestion, oedema and haemorrhages of the various organs. The only striking feature of the autopsy was a peculiar dark chocolate brown colour of the blood. As no diagnosis could be arrived at, the organs were sent to the chemical analyser, who detected *paranitraniline* in the tissues.

Case 2—B.A., was in a dazed condition, but responded to painful stimuli. There was no smell of alcohol to his breath. His temperature was 101°F, pulse rate 130 per minute, and respiration 38 per minute. The pupils were normal in size, and reacted well to light. There was a slight rigidity of the neck during flexion only, but Kernig's sign was not present. The superficial and the deep reflexes were normal and the planter response was flexor on both the sides. The tongue had a bluish margin. Besides this nothing abnormal was detected in the other systems. Within an hour of admission he developed a yellowish pigmentation of the palms and the soles which gradually spread to the other parts and deepened in hue as it spread. Simultaneously he developed a respiratory distress, and the tongue showed the characteristic leaden hue. He complained of a severe headache and within a short while he became disoriented in time and space and garrulous. He had a white blood cell count of 15,300 per c.mm. Polymorphonuclear neutrophils 70 per cent, basophils nil, eosinophils nil, lymphocytes 28 per cent, large mononuclears 2 per cent. No parasites were seen in the peripheral blood smear. His urine was of a dark yellow colour but showed no abnormal constituents. Bile salts and pigments were particularly looked for and found to be absent. His blood was of a dark chocolate brown colour, and retained its fluidity for over 48 hours so that the serum could not be obtained for determining the icterus index and the Van den Bergh reaction. On spectroscopic examination the blood which was of a dark chocolate brown colour was surprisingly reported to be showing absorption bands of oxyhaemoglobin.

On oxygen therapy and stimulant line of treatment the patient made a gradual recovery but the headache persisted for four days.

It was after he regained full consciousness that he told the story given at the beginning of this paper, which led to further investigations and a sample of the powder which they transported was obtained,

which on chemical analysis was found to be *paranitraniline*. Stomach washings and urine of B. A. and the alcohol with which his nails and skin were washed to remove the yellow discolouration were also sent for chemical examination but no *paranitraniline* was detected in them.

Going over the records of the K. E. M. Hospital, two more cases of *paranitraniline* poisoning admitted during the last ten years were found, which are described below.

**Case 3**—K. T., a Christian male, aged 38 years, employed in a dye factory returned from his work at about 6-00 p.m. on 15-12-41, and started vomiting incessantly. He was admitted in the hospital a little later in a collapsed and semi-conscious condition. When examined, the patient did not answer questions but reacted to painful stimuli, he was cyanosed, and the respirations were rapid and shallow. Any characteristic smell to his breath was not noted. His temperature was 97°F, pulse rate 110 per minute and respiration 30 per minute. Besides this nothing abnormal was detected in the clinical examination. Within 2 hours of admission his temperature rose to 101.2°F, but settled down to 98°F within 24 hours. His total white blood count was 7,200 per cu. mm., polymorphonuclear neutrophils 76 per cent, basophil 1 per cent, eosinophil nil, lymphocytes 23 per cent, and large mononuclear nil. On oxygen therapy and stimulant line of treatment the patient made a rapid recovery. The yellow powder with which he was working, was found to be *paranitraniline* on chemical analysis.

**Case 4**—M. J., a Christian male aged 45 years, employed in the same dye factory as K. T. (case no. 3) and staying with him, was admitted in the hospital at the same time, under similar circumstances. On examination he was found to be deeply comatose, and did not respond to painful stimuli. His temperature was 97°F, pulse rate 104 per minute, and respirations 15 per minute and Cheyne-Stokes in character. There was marked cyanosis, a slight rigidity of the neck, widely dilated and fixed pupils, and absence of planter response and deep jerks. His total white blood cell count was 12,100 per cu. mm., polymorphonuclear neutrophils 70 per cent, eosinophils nil, basophils 2 per cent, lymphocytes 28 per cent, and large mononuclears nil. The cerebrospinal fluid was normal. The patient regained consciousness after 48 hours of continuous oxygen therapy and symptomatic stimulant line of treatment, but was running an irregular temperature for 4 days with a maximum rise to 101.4°F, after which the recovery was complete and uneventful.

Yellowish pigmentation of the body was not observed in cases number 3 and 4.

#### DISCUSSION

*Paranitraniline* ( $C_6H_4NO_2NH_2$ , -nitro-amido derivative of Benzene) is a highly poisonous substance used in the preparation of red dyes. It is commonly used in textile industry but the reported cases of this poisoning are comparatively very few in medical literature, and it is with an idea of familiarising the practitioners with this syndrome that these cases have been reported. Lobo-Mendonca (1942)\*

\* Lobo-Mendonca, R.—Indian Medical Gaz. LXVII Nov. 1942, p. 678

has reported 8 cases from Bombay and described 6 of these cases in detail

Paranitraniline is a yellow powder derived from acetanilide, a coal tar preparation, and is the most poisonous of the aniline group of dyes. Whereas aniline poisoning occurs due to ingestion of the liquid, paranitraniline poisoning most often results from inhalation of the volatile powder or absorption of the powder from the unbroken skin, particularly when the skin is moist. However if the powder is ingested on an empty stomach, or with alcohol, absorption is rapid and an acute attack may be precipitated. The effective sites of action of this poison are the central nervous system and the blood. In the latter, it causes an alteration of the vital pigment, oxyhaemoglobin, into the inert methaemoglobin, which causes respiratory distress. In the central nervous system it causes a gradually progressive paralysis of the vital bulbar centres, which ultimately ends in death. In an acute case, the individual, most commonly towards the end of the day after cessation of work, experiences an irresistible feeling of progressive weakness and nausea, which may or may not be accompanied by vomiting, and abdominal pain. Very soon the victim is overcome by a feeling of giddiness which merges into drowsiness deepening into coma. The body becomes cold and clammy, a characteristic leaden hue appears at the tips of the nails, the tongue, and the lips, there is air hunger, the pulse becomes fast and feeble, and there may be a rise of temperature, particularly if the rectal temperature is recorded when the skin is cold and clammy. Mild cases recover from this stage but the more serious ones succumb to the effects of the poison either in a state of coma or sometimes they may develop convulsions before death. Besides causing this picture of acute poisoning, paranitraniline may also, by its chronic irritative action, cause eczema, cystitis, haematuria, malignant neoplasms of the bladder, vertigo, chronic headache and chronic bronchitis.

#### DIAGNOSIS

The various types of clinical pictures presented by this poisoning may be confused with (i) food poisoning, (ii) acute abdomen, (iii) meningitis, and (iv) acute hepatic failure with jaundice.

(i) *Food poisoning*—The incessant vomiting of sudden onset, particularly if occurring in a number of people at the same time, simulates food poisoning but the history of association with a yellow powder, with the appearance of cyanosis and the chocolate coloured blood, showing spectroscopic bands of methaemoglobin rules out food poisoning in favour of paranitraniline poisoning.

(ii) *Acute abdomen*—Pain in the abdomen, vomiting and fever may lead one to make a diagnosis of an acute abdominal catastrophe and unless the other signs like yellowish pigmentation, cyanosis, or methaemoglobinaemia appear or there is a definite history of association with paranitraniline the diagnosis may be extremely difficult.

(iii) *Meningitis*—The semi-conscious condition, slight rigidity of neck, headache, delirium and vomiting may suggest meningitis but the cerebrospinal fluid is normal and other characteristic signs like

the leaden cyanosis and methaemoglobinaemia make the diagnosis evident

(iv) *Acute hepatic insufficiency with jaundice*—This may be thought of because of the fever, vomiting and the yellow pigmentation of the skin but the urine does not show any evidence of bile salts or pigments, the conjunctivae are not pigmented, and the characteristic chocolate coloured blood and methaemoglobinaemia, with the history of association with paranitraniline may prevent the error being made

Poisoning with paranitraniline should be suspected when an individual who is associated with the textile industry, or any of its branches, is found in a state of semi-consciousness, with yellow pigmentation of the skin which can be cleaned with alcohol, and shows respiratory distress with a leaden hue of the nails, tongue and lips. The diagnosis is almost certain if the blood has a dark chocolate brown colour and shows spectroscopically the presence of a methaemoglobin. The diagnosis is confirmed by demonstrating the presence of paranitraniline or its oxydation product para-amino-phenol in the urine

#### TREATMENT—

The treatment of this condition is mainly symptomatic. The unconscious patient should be removed to the fresh air, saturated clothing should be removed, and the skin cleansed of any material, the body wrapped in blankets and kept warm. Respiratory embarrassment should be combated by continuous oxygen therapy or oxygen and carbon dioxide inhalations and if required a Drinker's apparatus should be used. Intravenous injection of 1 per cent methylene blue is indicated as in other cases of enterogenous cyanosis. The activity of the vital centres should be maintained with such stimulants as leptazol ( $1\frac{1}{2}$  to  $4\frac{1}{2}$  grains), nikethamide (15 c.c. to 5 c.c.), strychnine ( $1/30$  gr), or caffeine sodium benzoate ( $7\frac{1}{2}$  grs). Venesection, removal of 16-20 oz of blood, followed by transfusion of blood to rid the body of methaemoglobin, has also been advocated.

(My thanks are due to my chief Dr N D Patel, M.D. (Lond.), M.R.C.P. (Lond.) F.C.P.S. (Bom.) for permission to report these cases, and the Dean K E M Hospital for use of hospital records and to Dr V V Jadhav, M.B.B.S. and Dr S V Joglekar M.B.B.S. F.C.P.S. (Bom.) for the trouble taken in tracing the original powder and getting it chemically analysed.)

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# FACTS, FADS AND FANCY IN INTRAVENOUS MEDICATION\*

by

K V THAKKAR, L M. & S

Bhavnagar

My object in speaking to you to-day is to place before you a few most important facts relating to Intravenous Medication. First I would say, "Do it when you must" Do not use the method, simply because it is so easy to throw in a medicament into the blood stream. Do not take it as a fad but use it only if it is absolutely necessary and other routes of administration cannot be used. It would, thus, be the height of absurdity and recklessness to give orange juice intravenously for treatment of scurvy and yet this has been done! A physician<sup>1</sup> of South Africa has reported that he gave intravenous injections of raw unneutralized orange juice at intervals (10 cc in 150 cc of normal saline solution) to a patient and he reported that this procedure caused disappearance of all symptoms of scurvy and saved the patient's life. This was nothing less than a criminal use of a good method. It was a spectacular test for the patient's heroic resistance to a foreign agent. The oral route was here the proper route. Similarly in the great majority of cases of malaria, oral administration of quinine suffices. It is only in cases of cerebral malaria or in cases of acute pernicious malaria, especially when accompanied by constant vomiting that the question of injecting quinine arises.

## *Indications and Contra-indications*

Like drugs meant for oral administration, every drug meant for intravenous medication has its indications and contra-indications and these must be borne in mind before we decide to administer a particular medicament by the venous route. It is when these are disregarded and *because* these are disregarded that fatalities occur. L. J. Witte<sup>2</sup> has stated that every kind of intravenous injection, except normal saline, has at some time or other proved fatal. In other words, every medicament for intravenous use must have safety combined with efficiency and that there is and there can be no justification for using a remedy in which the two are not combined to a remarkable degree.

Even a most useful and widely used drug like glucose has its contra-indications, though few. While its indications are many and varied and its utility as a life-saving measure very great and the margin of safety very wide, under certain conditions, it has to be used with great care and caution. There was a case of phlegmasia alba dolens (White Leg) in a young lady of 30. The two doctors attending the case differed about the utility of a glucose injection and I was asked

\*A short talk delivered before the Mission Hospital Clinical Society of the Medical College Hospital, Vellore on 3-4-1945 Dr S. Gurubatham presiding.

to decide the point. While one believed in glucose almost as a panacea for all ills, the other saw no indication for it at all. As a matter of fact, not only was there no indication for glucose but in view of the presence of the thrombus in one of the veins of the right lower limb, there was a definite contra-indication, the reason being that even an injection of 20 c.c. of a 20% solution of dextrose has been known to produce a venous thrombus. Using 20 c.c. of 20 per cent of dextrose solution Stuber and Lang<sup>3</sup> observed changes in the coagulation time, glycolysis, alkali reserve, and protein and chloride content of the blood of a large number of healthy individuals and of patients with cardiac failure. The most notable and constant change was an acceleration of blood coagulation which was faster in patients with cardiac failure than in normal individuals. Other noteworthy changes in cardiac failure were increase in glycolysis and of lactic acid, also variation in mineral content, disturbed albumen-globulin ratio with increase in the globulin and fibrinogen fractions, increase in thrombocytes, associated with a decrease in their electrical charges and agglutination of platelets. All changes in blood chemistry were more extensive in patients with congestive failure than in the normal. Collectively, the phenomena observed were characterized as profound physico-chemical changes in the blood, which would favour the formation of thrombi and emboli. Again there are several drugs and preparations which can both be used intramuscularly or intravenously e.g., ergometrine, mersalyl and so many more. It is better therefore to use them intramuscularly first before resorting to the intravenous route. Recently several workers have reported deaths after intravenous injections of mersalyl.

Then again as regards every drug meant for intravenous medication, one has to bear in mind the following factors —

- (1) Its dose, minimum and maximum
- (2) The necessary amount and nature of the diluent best suited for its administration
- (3) The various affections in which it is useful
- (4) Contra-indications
- (5) Special precautions, if any, which it is necessary to observe before and after using the drug
- (6) In the case of certain drugs, like quinine or neoarsphenamine even the time to be taken in injecting a particular amount is a detail of very great importance

Then again there are the dangers arising out of air embolism and a rapid rate of injection. The danger of air embolism is very small, even negligible, when one thinks of the way in which and the extent to which the danger is trotted out. Harprasad of Bikaner<sup>4</sup> deliberately injected 3 c.c. of air into his patients and no harm came. Namee<sup>5</sup> injected upto 10 c.c. of air into own veins and came to the conclusion that the insufflation of air upto 10 c.c. during intravenous injections is quite harmless. Several letters appeared in the Indian Medical Gazette, many years ago, which I have collected and discussed elsewhere at length<sup>6</sup>. Though

all this proves the harmlessness of a few bubbles of air in a syringe or a gravity apparatus, it does no good to the patient and all air should be excluded from an intravenous apparatus. As Riddell<sup>7</sup> says "In the course of a transfusion, then, the entrance of a few bubbles of air need not be a cause of alarm, although they can hardly be regarded as evidence of a good technique."

But as regards the speed of injection, I must say, matters stand differently. There are three conditions where speed in injection is definitely and specifically indicated, viz, cholera asiatica, surgical shock and haemorrhage. In cholera<sup>8</sup> the speed of injection of hypertonic saline can be upto 4 oz per minute. Four pints can thus be given in 20 minutes. Some of us have treated at one time or another, cases of cholera with hypertonic saline and noticed how the infusion of a few pints of the hypertonic saline transforms an absolutely moribund patient from a lifeless into a lively being, conscious of his surroundings, a transformation which can never be forgotten by those who have seen it personally. Similarly in surgical shock and haemorrhage it is necessary to administer large amounts of blood or plasma in a few minutes in order to bring the blood pressure to a normal level, the drip may be brought into use after that, but barring these urgent indications, the bullock-cart standard of pace must be maintained in all intravenous work.

In my opinion, the speed factor is the one factor which has caused more deaths than any other. In a paper<sup>9</sup> which I read before the XXth Session of the All-India Medical Conference in December 1943, on a Plea for a Slow Rate of Injection in Intravenous Work, I quoted the following case from the practice of a colleague —

Patient X, emaciated and anaemic, due to chronic malaria, had a septic sore in the leg, for which he was given 2 c.c. of a watery solution of iodine intravenously. The patient died on the table soon after the injection. What could be the cause of death? Not being present at the time of injection, it was a surprise to me how such a small injection could cause the patient's death. But it did, similar deaths have occurred after injections of neosalvarsan, quinine and other potent medicaments. But a watery solution of iodine could hardly be classed as a powerful remedy. One could well understand a large bulk of intravenous fluids causing embarrassment and failure of the heart, but how could 2 c.c. of a watery solution of iodine cause a patient's death?

The fact is that in the patients suffering from chronic sepsis, the functional efficiency of the myocardium is affected by long standing anaemia and severe toxæmia and deaths do occur when such patients are injected a large amount of fluid at a rapid rate. After all the property of contraction of the heart muscle belongs to the length of the muscle fibres, and in cases of chronic sepsis and anaemia the heart fibres already stretched to their fullest extent have little capacity to stretch further. Two typical experiments, selected from a large number carried out by Hirshfield and Hymen<sup>10</sup> illustrate this point very clearly. (a) An animal received 25 c.c. of a hypotonic (0.1%)

saline solution at the rate of 1 cc per minute without any effect on the blood pressure, whereas the same animal showed symptoms of circulatory embarrassment from a rapid injection of 2 cc of the same solution (b) 10 cc of horse-serum was infused slowly into guinea-pigs sensitized ten days previously. No evidence of anaphylaxis occurred. Later 0.1 cc was injected rapidly and the animals died of typical shock. Danger thus lies much more in speed of administration than in the amount transfused.

The point is to go slow. The heart is strained if it is suddenly presented with a large blood volume, especially when the myocardium is in a damaged condition. And it is with the recognition of the fact that danger lies much more in speed of administration than in the amount transfused that the intravenous drip has come into existence and that massive transfusions can be safely given to an anaemic patient, if they are given slowly enough (Marriott and Kékwick)<sup>11</sup>. It is one of the advantages of a very slow administration that if cardiac failure does develop, there is usually plenty of time to recognize it and to stop before the condition has become irreparable<sup>12</sup>. But the question immediately arises what is the standard rate for a slow injection? Different workers have given different rates. Hirschfeld<sup>13</sup> and his co-workers suggest 1 cc per minute for amounts less than 100 cc and 2 to 3 cc for amounts above 100 cc. Titus<sup>14</sup> puts it down as 4 cc and workers at the Mayo Clinic<sup>15</sup> at 10 to 20 cc. Others put it at even 30 cc per minute. There is thus no uniformity about the standard slow rate but it is evident that hypertonic solutions should be given more slowly than isotonic ones. Substances like saline and dextrose may be given more rapidly than neosalvarsan and this again may be given more rapidly than potent substances like quinine. As regards quinine, Manson-Bahr<sup>16</sup> has stated that 2 to 4 minutes should be spent in injecting one grain of quinine bihydrochloride. "I feel certain that it is sound to lay stress on the importance of the speed factor (2 to 4 minutes per grain)." This means it is necessary to have a chair to sit down and a watch to time, while giving the injection slowly at the above rate. An ideal rate of injection should eliminate the possibility of speed shock yet allow the medicament to exert its specific effect.

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# WHAT'S IN A NAME?

by

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For quite a long time past I have raised my voice in protest against the use of proprietary names for medicines in every day use. My chief reason for this has been that the practice causes a great deal of extra worry and uncertainty for the hospital dispenser and (or) the chemist shop dealer. I am, therefore, glad to notice attention being called to this practice for another reason, viz., that of the extra cost involved. In the January 20, 1945, number of the British Medical Journal the writer makes the startling statement that "a large New York Hospital recently instructed its dispensary to supply for all proprietary medicines ordered for patients the equivalent products described in the United States Pharmacopoeia. This saved the hospital no less than £12,500 in one year." The question, 'What's in a name?' is fully answered by the above experiment. In these difficult days and in a charitable hospital, above all, it surely behoves each one of us to consider expense. Let me give a few examples which have come to my notice. Ergotamine Tartrate is, as all clinicians know, a drug which has a direct action on the sympathetic part of the autonomic nervous system, and is of great value, therefore, in cases of hyper-sympathotonia and in conditions where an action antagonistic to that of Adrenalin is indicated. Though this is the case, I have never been able to obtain Ergotamine Tartrate except in the form of a proprietary article. Under the name of Neo-gynergen it is to be obtained with Ergotine Tartrate, and as Bellergeral, in combination with Atropine (also given a proprietary name). Obviously the first named is intended for gynaecological use only and the second as an antispasmodic in cases of hypersensitive bowel conditions. One may not want either the added Ergotine or the Atropine, nevertheless without one or other of these he cannot have the desired drug, viz., Ergotamine Tartrate\*. No doubt the above is a glaring example of how the prescriber is at the mercy of the drug manufacturer but other situations no less troublesome must be the experience of all who try to escape from the net woven by manufacturing chemists for the exploitation of their own particular brand of a particular drug. Recently I ordered Sulphanilamidum B.P. This was not dispensed, the reason being given that it was not stocked. Yet on making enquiries I found that both Prontosil album and Proseptine could be had. The dispenser was not aware that these were simply proprietary names for an official sulphonamide preparation, namely, sulphanilamide. Again, very recently I had occasion to prescribe Cinchophenum B.P., this drug likewise was not known, whilst on enquiry I

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\* It is official in U.S.P. It is not official in the B.P. Gynergen is only ergotamine tartrate

found that the proprietary names agotan (Howard) and atophan (Scheering) were quite well known Cinchophen under its proper official name had never been heard of and the dispenser quite sincerely asked "was it a preparation of quinine?" One need hardly give further examples In this hospital we have made a beginning and we are now asking for *nikethamidum* B.P. and have dropped the numerous proprietary names for this drug Our only trouble being that for a time we shall have to be content to order nikethamide and to receive anacardone, coramine, or some other proprietary "synonym" In the case of *leptazolium* (B.P. 3rd add.) again it is to be hoped that cardiazol (knoll) will sink into oblivion. Leptazol chemically is pentamethylene-tetrazole  $\text{CH}_2\text{CH}_2\text{CH}_2\text{C}(\text{N})_2\text{N}(\text{N})_2$  and it is unfortunate that the U.S.P. has named this synthetical preparation metrazol At this point one would like to put in a plea for making use of the same name in both U.S.P. and B.P. Indian stockists cannot be expected to know that leptazol and metrazol are both of them pentamethylene tetrazol (or cardiazol-knoll) and that the first is a B.P. name and the second U.S.P. name Moreover, even where the name is the same, sometimes the chemical formula is different As an example we may name acriflavina, N.F.B.P. (add I) which in the U.S.P. is a basic and neutral preparation, whilst in the B.P. it is an acid salt, i.e., it contains HCL in its molecule and, as the B.P. states, is a mixture of the hydro-chlorides of 2 8-diamino-10-ethyl-acridanum chloride and 2 8-diamino-acridine (B.P. add I 1936, page 6) This may seem a small matter, but conditions arise where a neutral salt is preferable, i.e., for intravenous injections, and at other times the acid salt is better, e.g., for bladder irrigation where the organism is B.Coli and it is desirable with mendeleeff acid treatment to keep the urine at about pH 5 Writing of this the United States Dispensatory (23 edition page 61) says, "We prefer the American name to that of the British Pharmacopœia as the latter title is capable of confusion Because of the deep colour of a solution of this latter salt it is difficult to reveal its acid character by any of the ordinary indicators, but its acidity can be demonstrated by its power of decomposing carbonates"

To return to our subject Is it not the case that we make use of these proprietary drugs in order to save ourselves time and trouble? We are given literature about cardiazol We are told that never before or since or likely ever will there be a respiratory stimulant to equal "cardiazol" and when to this parent name others are added such as cardiazol-ephedrine, cardiazol-dicodid, cardiazol-strophanthin, we are completely seduced, and take the short cut to avoid the problem of working out and writing down the official preparations which in every case correspond to these proprietary drugs

*Mersalylum* B.P. U.S.P., here we are fortunate in having one name in both official standards for the organic mercurial formerly known as Salyrgan (Bayer) and Neptal (May & Baker) *Mepacrinae* hydrochloridum (B.P. add III), *mepacrinae* methane sulphonas (B.P. add III), *pamaquinum* (B.P. add IV) These quinine substitutes are now official, let us then no longer use the names, e.g.,

atebrin (Bayer), quinacrine (May & Baker), atebrin musonate (Bayer), and plasmo-quine (Bayer)

In the seventh and latest addendum of the B.P., benzedrine has taken its proper name *amphetamine* which is chemically phenyl-amino-propane,  $C_6H_5CH_2CH.NH_2CH_3$  and Nembutal becomes *soluble pento-barbitone*. This preparation is in both the U.S.P. XI and U.S.P. XII as pentobarbitalum Sodicum. Both in the U.S.P. and the B.P. the chemical name is given as sodium ethyl-methylbutyl-barbiturate, so even though we forget 'nembutal' we have still two official names to describe the same synthetical drug.

Another barbiturate to be brought to the front by the B.P. 7th addendum is pentothal. This is now to become *soluble thiopentone*. Pentothal sodium of the N.N.R. (New and Non-official Remedies) of the United States, is sodium ethyl-methylbutyl-thiobarbiturate. Chemically the only difference between these two barbiturates is that of sulphur atom which in the case of the latter preparation enters the barbiturate complex in place of an oxygen atom.

All that we have said applies equally to the whole of the sulphonamide group, to the vitamins and hormones likewise. Considering these things we conclude that the sea is daily becoming deeper, the only way to avoid being carried down into it by the ever increasing burden of proprietary names, is to keep above the waves upheld by a knowledge of the nature of the official preparations, their inclusive range and acknowledged purity.

### Editor's Note —

We entirely agree with Dr. Draper in his protest against the use of proprietary names for official drugs of the B.P. or U.S.P. We have previously printed the official names for some new drugs (*Indian Physician* Vol I, page 109) and we reprint this list below with some additions for the convenience of our readers. We have also printed short reviews of the fourth addendum to the B.P. 1932 and the fifth addendum to the B.P. (*Indian Physician* Vol I, pages 104 and 188) and have also printed a review in detail of the twelfth 1942 edition of the U.S.P. by Dr. Paranjpe under the title "Recent Advances in Therapeutics" (*Indian Physician*, Vol II, pages 225, 263, 323) giving information about the newer drugs and their official names. The habit of using proprietary names for common drugs appears to be deep rooted in the practitioners and the worst culprits are perhaps the consulting physicians, who appear to us as if they were the registered agents of the pharmaceutical concerns. The constant flow of manufacturers' circulars eulogizing their particular wares, the innate mental laziness of doctors to enquire about the nature, composition and the pharmacological action of these preparations and the difficulty of obtaining B.P. and U.S.P. preparations in the market on prescriptions are probably at the root of this undesirable practice. This clearly stresses the necessity of an act requiring that all drug stores, pharmacies and dispensaries should be in charge of qualified pharmacists, holding a state licence to practice.

A LIST OF NEW OFFICIAL OR APPROVED NAMES  
FOR SOME DRUGS

<i>Official or Approved Names</i>	<i>Proprietary Names</i>
Acetylsalicylic acid	Aspirin
Amethocaine hydrochloride	Decicain
Amphetamine Sulphate	Benzedrine sulphate
Biliselectan	Pheniodol
Bromethol	Avertin
Carbachol	Doryl
Cataplasma kaolini	Antiphlogistin
Chiniofon	Yatren
Diodone	Perabrodil
Diphenan	Butolan
Dithranol	Cignolin
Hexazole	Thriazole (Azoman)
Hexobarbitone	Evipan
IodoxyI	Uroselectan—B, Pyelectan, Uropak
Leptazol	Cardiazol
Menaphthone	2-methyl-1 4-naphtho- quinone
Mesulphen	Mitigal
Mepacrine hydrochloride	Atebrin, Quinacrine
Mepacrine methanesulphonate	Atebrin musonate
Nikethamide	Coramine
Oleum iodisatum	Lipiodol, Neohydriol, Iodotal
Pethidine hydrochloride	Dolantin
Phenobarbitone	Luminal, Gardenal
Pholedrine	Veritol
Pamaquin	Plasmoquin
Phemitone	Prominal
Soluble phenytoin	Epanutin, Eptoin, Sodium diphenylhydantoinate, Solanton, Soluble Dilantin
Soluble barbitone	Medinal, Embinal
Sulphacetamide	Albucid
Soluble hexobarbitone	Evipan sodium
Stibophen	Fouadin
Suramin	Germanin (Bayer 205)
Theophylline Ethylenediamine	Cardiophyllin, aminophyllin



# Critical Notes & Abstracts

## NICOTINIC ACID AND GINGIVITIS

Coulson, Ellinger, and Smart (B M J Jan 6, 1945, pp 6-8) describe a test which is considered to give a fairly reliable indication of the state of Nicotinamide metabolism. The differences observed in the amount of nicotinamide metho-chloride in the urine of normal subjects and in the urine of those with various types of gingivitis, though statistically significant, was not considered to be of etiological importance, since other factors were observed to have a marked influence on the results. The results obtained with this test were related to standards of feeding. Those getting the best food eliminated the greatest quantities of nicotinamide methochloride after a test dose of 100 mg nicotinamide. Among subjects who had similar standards of feeding, i.e., who were in the same economic or social class—the response of urinary methochloride to 100 mg of nicotinamide was the same whether gingivitis was present or not. They conclude that nicotinamide deficiency probably did not play any part in the development of gingivitis of any type among the subjects examined.

## L. S. R. IN INFECTIVE HEPATITIS AND IN MALARIA

Paul Wood (BMJ Jan 6, 1945, p 9) recognizing the difficulty of diagnosis between clinical malaria and the pre-icteric stage of infective hepatitis, suggests that in the erythrocyte sedimentation rate there is a simple laboratory test at our disposal as an aid in the differentiation between the two diseases. He found the behaviour of the E S R in 35 unselected cases of infective hepatitis, normal during the first week or ten days, whether there was fever or not. It rose slowly and steadily during the period of biliuria, to reach a maximum between 15 and 30 mm in one hour (Wintrobe). During the stage of recovery, when the urine was free from bile, the E S R returned slowly to normal, a minority of cases showing further acceleration before this occurred. The behaviour of E S R in malaria, M T, B T, fresh attacks, or cases of relapse, is in sharp contrast. During the first 10 days the E.S.R. ranged between 12 and 60 mm in one hour, in 84 per cent of 51 cases. Only in 4 cases was it below 10 mm in one hour. He concludes—The E.S.R. is of value in the early diagnosis of infective hepatitis, especially in its differentiation from clinical malaria. In the first 10 days of infective hepatitis about 85 per cent of cases have an E.S.R. below 10 mm in one hour (Wintrobe). In the first 10 days of malaria about 85 per cent have an ESR above 10 mm.

An ESR above 20 mm in one hour during the first week of a pyrexia of unknown origin practically excludes infective hepatitis, on the other hand, such a reading occurs in about two-thirds of all cases of clinical malaria during the first week.

The E.S.R. serves to distinguish clinical malaria from short term fevers of uncertain etiology. In malaria the acceleration is maintained for at least two or three weeks in about 84 per cent of cases, in short term fever the ESR is commonly normal within one or two weeks of the onset.

**BREATHING, ABDOMINAL BELT AND CORONARY CIRCULATION**

R H Dixon in a letter (B.M.J Jan 6, 1945, p 27) remarks that the death rate from angina pectoris and coronary thrombosis has rapidly risen in the last 30 years. He writes "Can nothing be done to check this increased mortality? Certainly no drugs or dieting will help. Is there any physical method that would help? It is possible that sustained increase of well-oxygenated blood to the heart would help. The problem is to produce this condition, the left ventricle, elastic arteries, and gravity help the outflow to the tissues, but the return of the blood to the heart is retarded by gravity and the lack of elasticity and poor valves in the veins, to the rescue comes the suction action of the thorax during inspiration. Unfortunately in so many men the thorax scarcely moves during inspiration, but it is otherwise in most women. If physical means will help, the exercises to be given are —

(1) To put most of the body weight on the balls of the toes when standing and also when sitting. This stance tones up the muscles of the feet, the legs, the thighs, and the abdominal muscles, and thus helps veins and lessens the action of gravity.

(2) To see that the thorax moves sufficiently when breathing. This is done by keeping the shoulders tightly back and slightly down and holding them steady there during inspiration and expiration. To keep the shoulders tightly back is done with least effort by getting the pull in the back just below the axillae.

(3) In addition to the above, deep thoracic breathing should be undertaken, say, twice a day, and the range of movement should be checked in front of a mirror to be sure the thorax is really moving.

Naturally this idea and its results cannot be proved but it is common sense to ensure plenty of blood to the arteries and muscles of the heart if the heart is to keep from disease. All, especially men who fear that these complaints may be their weakness, would do well to follow these simple suggestions of breathing and stance during the day."

In a second letter (B M J Feb, 24, 1945, p 276) the author stresses the importance of relaxing the chest muscles in order to obtain a free range of thoracic movement. "The first exercise is to breathe fully in and out deeply through the nostrils, the shoulders being first drawn back and down, the second is to inhale fully and then hold the breath for 15 to 60 seconds or longer, and the third is to exhale completely and then hold the breath for 15 to 60 seconds or longer. By keeping the shoulders back and down when standing, sitting, writing, and stooping, the necessary movement of the chest is carried on unconsciously and the same happens at night, when lying, say, on the right side if the left elbow is placed just behind the long axis of the body. When standing the weight of the body should be on the balls of the toes."

A surgeon (B M. J., Jan., 20, 1945, p 97) who has personal experience of relief from anginal pain draws attention to Dr A T-Todd's suggestion regarding the influence of respiratory insufficiency in pro-

ducing cardiac symptoms and pathological lesions (*Treatment of some Chronic and Incurable Diseases*, Wright, Bristol, 1937, p 91) Todd recommends regular breathing exercises in order to increase the chest expansion, and thus to ensure the sufficiency of the respiratory pump. In his opinion, insufficiency of the respiratory pump produces inadequate aortic pressure, defective irrigation by the coronaries, gradually increasing coronary sclerosis, and ultimately organic changes in the myocardium.

#### TODD'S BREATHING EXERCISES

These are to be carried out standing erect, and breathing is to be through the mouth, not the nose, a breath is not to be held at all, but released as soon as maximal. Strong efforts to gain large volumes are to be deprecated, the slightest amount of forcing only is advised.

1 Interlock the fingers and apply the hands with the palms to the upper abdomen, the thumbs to be extended fully, the upper borders of the thumbs to lie parallel with and half an inch below the chondrial margins. The hands are to be used as indicators of abdominal movement only, no pressure is to be made. The patient now inspires deeply and tries to contract his upper abdominal muscles so that with inspiration the palms move backwards, and forwards with expiration but this takes time and practice. This exercise acts especially on the upper thoracic respiratory muscles.

2 Arms by the sides. With slow deep inspiration the hands and arms to be raised laterally, palms directed outwards, and meet above the head just as inspiration is complete, then arms descend and touch the thighs at the end of expiration. This exercises the lower thoracic muscles.

About three of each is enough at first, but the number should be slowly increased until they last for five minutes. The patient is encouraged to practice them several times each day.

#### ABDOMINAL BELT

Todd also advises (p 100) a low-fat diet and an abdominal belt to make the patient use efficiently his thoracic respiratory muscles. The belt is to be worn night and day, as a continual reminder of its purpose. Kerr, Prof of Medicine, University of California Medical School, also advocates a special abdominal belt in cases of emphysema, and in cases of angina pectoris—(*The treatment of Angina Pectoris by Methods which appear to promote more adequate Filling of the Heart*, Amer Heart Jour 16, 544, 1938). His belt, known as the Kerr-Lagen Belt, is fully described in *Body-Mechanics* (Lippincott, 1941, pp 122-125). Kerr supplements the use of the abdominal belt with dietary restrictions. He hopes that this method of promoting more adequate filling of the heart might in some measure prevent or postpone coronary thrombosis. Leaman reports encouraging results from the use of abdominal belt (*Management of the Cardiac Patient*, 1941, p 252) in coronary disease with anginal pain of long duration. Kerr states that in a series of almost 300 patients with anginal pain, the attacks have been prevented almost uniformly. Many sufferers have been restored to an active business or professional life.

## Book Reviews and Notices

आधुनिक नेत्ररोगविज्ञान शास्त्र (हिन्दी) — by D D Sathaye, F.R.F.P.S (Glasgow), Vol I Part 1, pp 306 with 200 illustrations many in colour, 1945 published by V D Sathaye, Indian Journal of Ophthalmology, 802, Narayan Peth, Poona City, Price Rs 15

Many great books are written in His Majesty's Prisons This one is a new addition Following the footsteps of his political gurus, Tilak Maharaj and Gandhiji, Dr Sathaye wrote it during his last stay in the prison as his majesty's guest The writing of a treatise on diseases of the eye was planned by Dr Sathaye many years ago, a draft was prepared in English and in Marathi, but it was only leisure in the jail that enabled him to write the system in Hindi for the benefit of all India The volume is published with the blessings of Mahatmaji who hopes that it will be of great value to the ophthalmic physicians

Dr Sathaye's is indeed a very praiseworthy effort to write a treatise in Hindi on a difficult technical subject like the science dealing with diseases of the eye in all their aspects, for the benefit of thousands of students and others who do not know any foreign languages and yet who are desirous of availing themselves of the latest progress in scientific knowledge relating to this branch This book in Hindi—the Indian national language which is understood practically all over India—supplies that long and keenly felt want Dr Sathaye is to be congratulated on the success he has achieved in enriching the Hindi scientific literature

The presentation of the material, the printing, the original drawings and the colour-prints, and the general get-up of this volume are excellent, and reflects very creditably on the author and the printers alike for its neatness

In this volume, the first part of volume I, are given the anatomy, the embryological development, the methods of ophthalmometry, the medico-legal aspects and the history of the emergence of this branch of science from the dawn of civilisation

The author proposes to publish three volumes The first volume is divided in two parts The second part of vol I will deal with physiology of the eye and errors of refraction, the second volume will contain diagnosis and treatment of eye diseases, and the third volume will deal with operations on the eye The whole set of four volumes, when completed, will be a respectable addition to the library of books on medical subjects in an Indian language

We have nothing but whole-hearted praise for the publication and in our judgment no medical library, and no Indian medical system practitioner of the speciality of the diseases of the eye can afford to remain without this authoritative and encyclopaedic set of volumes

—S K V

**The Year Book of Pediatrics**, Edited by I. A. Abt, and A. F. Abt pp 448, 1945, The Year Book Publishers Inc. Chicago Price \$3.00

This 1944 year book of pediatrics maintains the usual excellence typical of this series of annual publications from Chicago. We heartily recommend this volume to all practitioners interested in diseases of childhood, and to all medical libraries.

We draw special attention to the articles dealing with recent advances in Rh Factor, anaemias in childhood, erythroblastosis foetalis, childhood tuberculosis, problems of rheumatism, Coeliac syndrome in children, and articles dealing with poliomyelitis.

**Principles of Unani Medicine** by Hakim Ahmed Husain L.I.M. pp 107, 1942, published by S. Husain, 7 Perumal Chetty Street, Vepery, Madras. Price Rs. 3.

This small book is published to supply the need for knowledge about Unani System of Medicine in brief, in a connected and easily understandable way. As the name implies, the word 'Unani' means originating from 'Unan', i.e., Greece, and the present-day Muslim system of medicine is an elaborated and enriched version of the original Greek system. This enrichment was mainly due to the efforts of Ibne-Sina or 'Avicenna' and his followers in the tenth and eleventh Christian centuries.

Of recent years, since the resurgence of Indian Nationalism and increased instalment of self-government, Indian systems of medicine are again taken out from cold-storage and given Governmental support and the author, a Fellow of the Academy of Indian Medicine and Member of Eastern Medical Association of Southern India Madras, has availed himself of the opportunity to revive the knowledge of Unani medical system.

The book is divided into two parts. Part I deals with bodily structure, its organs and their functions, the food, drink and environment that affect it and the signs, temperamental and pathological, which help in diagnosis. Part II deals with general hygiene and principles of treatment.

To all those who are interested in Unani system of medicine, the book will afford valuable information. For comparison, students may refer to "A Treatise on the Canon of Medicine of Avicenna, incorporating a translation of the First Book" by O. C. Gruner, M.D. (London), published by Luzac & Co., London (1930). —S. K. V.

# Reflections & Aphorisms

VICTORY

"Let us not be discouraged The direction of our vision is everything, and after weltering four years in chaos poor, stricken humanity still nurses the unconquerable hope of an ideal state "whose citizens are happy absolutely wise, all of them brave, just and self-controlled all at peace and unity, and in the enjoyment of legality, equality, liberty, and all other good things" Lucian's winning picture of this "Universal Happiness" might have been sketched by a Round Table pen or some youthful secretary to the League of Nations That such hope persists is a witness to the power of ideals to captivate the mind, and the reality may be nearer than any of us dare dream If survived, a terrible infection, such as confluent smallpox, seems to benefit the general health Perhaps such an attack through which we have passed may benefit the body cosmic After discussing the various forms of government, Plato concludes that "States are as the men are, they grow out of human characters" (Republic, Book VIII), and then, as the dream-republic approached completion, he realized that after all the true State is within, of which each one of us is the founder, and patterned on an ideal the existence of which matters not a whit Is not the need of this individual reconstruction the Greek message to modern democracy? And with it is blended the note of individual service to the community on which Professor Gilbert Murray has so wisely dealt

With the hot blasts of hate still on our cheeks, it may seem a mockery to speak of this as the saving asset in our future, but is it not the very marrow of the teaching in which we have been brought up? At last the gospel of the right to live, and the right to live healthy, happy lives, has sunk deep into the hearts of people, and before the war, so great was the work of science in preventing untimely death that the day of Isaiah seemed at hand, when a man's life should be "more precious than fine gold, even a man than the golden wedge of Ophir" There is a sentence in the writings of the Father of Medicine upon which all commentators have lingered —

*The love of humanity associated with the love of his craft—philanthropia and philotechnia—(Ouevres completes d'Hippocrate, par E Littré IX, 258)—the joy of working joined in each one to a true love of his brother Memorable sentence, indeed! in which for the first time was coined the magic word "philantropy" and conveying the subtle suggestion that perhaps in this combination the longings of humanity may find their solution, and Wisdom—Philosophia—at last be justified of her children "*

—WILLIAM OSLER (1849-1919)

\*

"Medicine is called upon to prepare for the era of peace. In the midst of the terrors of war she and she alone is officially called upon to be present on the battlefield as the deputy of humanity, the representative of peace. Without distinction she takes friend and foe alike under her arm to heal the bloody wounds, tend the injured limbs, and cool the thirsty lips. In the powder smoke of battle she unfolds the banner with the red cross which all civilized nations have now recognized as a sign of immunity. Thus she erects a sanctuary for the wounded, protecting him from further attack and assuring him skilled assistance. Her frail tents and barracks arise wherever there is need, as shelters of human love and mercy.

We must prove ourselves worthy of the distinction that those in power have given us. We shall be the high priests of humanity at war, giving blessings to all. But let us remember that the greater problem cannot be solved in war, rather, patient and arduous work during peace time will be necessary to establish humane understanding and intercourse as the basis for all public relations and the object of all private endeavour. More especially in this war we dare not forget that we are fighting that people which, after our own, has made the greatest sacrifices to free mankind and with which, united in peace and stimulated by competition, we could produce the finest of human works. May all science exert its influence when the peace is won to foster reconciliation and a comprehension of our community of interests."

—RUDOLF VIRCHOW (1821-1902)

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#### MEDICAL TEACHING

"Uncorrelated factual information is quite unsuitable for the undergraduate student. What he needs to learn is the principles of clinical examination, and a string of facts has no more relevance to them than a list of Solomon's concubines to the study of theology."

"A good deal of nonsense has been written lately about the alleged lack of powers of observation shown by modern medical students. Most of the writers would be unable to say what was the colour of the eyes of the last person they saw, what side he parted his hair, or whether or not he had a moustach, in spite of the fact that they may be quite good doctors."

"Medical diagnosis is a specialized type of observation, like judging the points of a cow or the weight of a cheese. The duty of medical teachers is to inculcate this specialized type of observation, and yet keep alive in their pupils the generalized and unconventionalized powers of observation which are characteristic of an intelligent small boy. This is not an easy task."

# The Indian Physician

VOL IV NO 7

JULY 1945

WHOLE NO 43

## Original Contributions

### P-P INTERVAL AND RETROGRADE (V-A) CONDUCTION IN COMPLETE HEART BLOCK

by

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Erlanger and Blackman (1909) from a study of heart block in experimental animals observed that ventricular contractions disturbed the auricular rhythm although there was complete auriculo-ventricular block Hecht (1914) described this condition clinically in a child Wilson and Robinson (1918) observed the disappearance of this arrhythmia by exercise and the P (auricular complex) that followed the R (ventricular complex) was abnormal Lewis (1925) noted this irregularity more often in 2:1 heart block Ellis (1932) described this irregularity in six of the 43 cases of complete heart block Carter (1932) Levine (1936) and Schnijker (1940) have also observed this phenomenon Parsonnet and Miller (1944) from a study of 28 cases of complete and 10 cases of incomplete heart block observed that the P-R-P\* interval was shorter than the P-P interval in 50 per cent of the cases of complete heart block, the P-P interval was shorter in 71 per cent and in the remaining 42.9 per cent there was no correlation between the intervals In incomplete heart block P-R-P was shorter in 50 per cent, P-P was shorter in 20 per cent and in the remaining 30 per cent there was no correlation

Engelmann (1895 and 1903) showed that retrograde conduction is one of the normal functions of the conducting pathway in experimental animals Bain (1941) observed retrograde conduction from ventricle to auricle in two of the four cases of complete heart block associated with bilateral bundle branch block Pardee (1942) observed in some of his cases of complete heart block the occurrence of retrograde conduction from the ventricle to the auricle Winternitz and Langendorf (1944) collected nineteen cases from the literature (including two of Bain 1941), the first case being that of Cohn and Fraser (1913), and reported six more cases

\* P R P interval denotes the interval between two auricular contractions when ventricular contraction occurs between the two

P P interval denotes the interval when there is no intervening ventricular contraction



Raman (1944) reported six cases of complete heart block in which ten electrocardiograms of four cases were taken. These ECG were re-examined with a view to find out whether similar changes could be made out in the P-P and P-R-P intervals and whether there is any evidence of retrograde conduction. The findings are as follows.

Case 1—Syphilitic myocarditis with commencing aortic regurgitation in a Hindu male aged 40 years.

TABLE 1 E.C.G. (Fig. 1)

		P—P in seconds	P—R—P in seconds	P—R & R—P in seconds
Lead I	P1—P2	0 72		P3—R1 0 04
	P2—P3	0 72		P5—R2 0 32
	P3—P4		0 72	P7—R3 0 48
	P4—P5	0 72		
	P5—P6		0 72	
	P6—P7	0 72		
	P7—P8		0 72	
	P8—P9	0 72		
Lead II	P1—P2	0 84		P2—R3 0 40
	P2—P3		0 72	P4—R3 0 48
	P3—P4	0 80		
	P4—P5		0 72	P6—R4 0 64
	P5—P6	0 80		
	P6—P7		0 72	
Lead III	P1—P2	0 80		P2—R1 0 44
	P2—P3		0 72	P4—R2 0 52
	P3—P4	0 80		P6—R4 0 80
	P4—P5		0 72	
	P5—P6	0 80		
	P6—P7		0 72	

Lead I did not show any change in the P-P and P-R-P intervals but leads II and III showed definite reduction in the P-R-P intervals. The abnormal appearance of P5 in lead II might be taken as instrumental.

Case 2—A case of atherosclerosis and senile myocarditis in a Hindu male aged 60 years.

TABLE 2 E.C.G. (Fig. 2)

		P—P in seconds	P—R—P in seconds
Lead I	P1—P2		0 68
	P2—P3	0 68	
	P3—P4		0 68
	P4—P5	0 68	
	P5—P6	0 68	
	P6—P7		0 68
	P7—P8	0 68	
Lead II	P1—P2		0 68
	P2—P3	0 68	
	P3—P4		0 68
	P4—P5	0 68	
	P5—P6		0 68
	P6—P7	0 68	
Lead III	P1—P2	0 68	P2 and R1 are superimposed
	P2—P3	0 68	
	P3—P4	0 68	
	P4—P5		
	P5—P6	0 68	
	P6—P7		

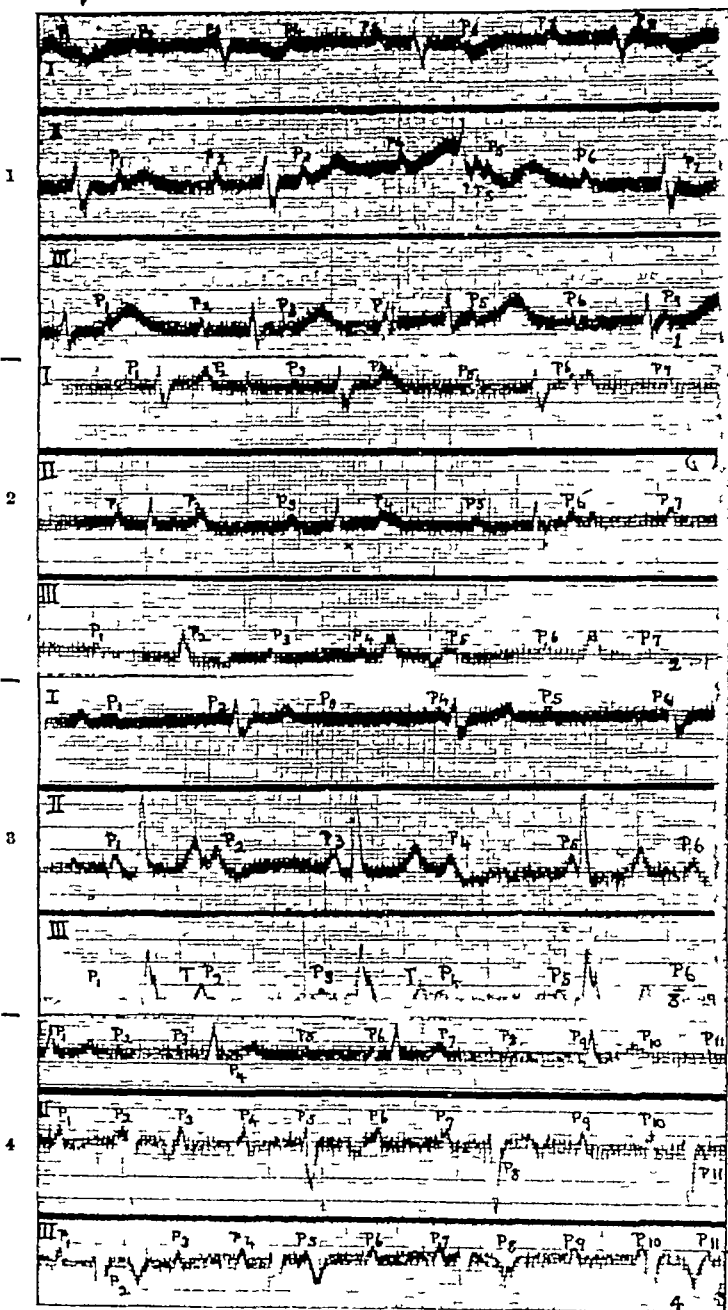


Fig 1 (Case 1) Leads I, II and III showing complete heart block auricular rate 72 and ventricular rate 48 per minute P R P interval is shorter than P P interval in leads II and III The contour of P5 in lead II has been modified by the disturbance of the fibre (instrumental) Arborization block is present in addition

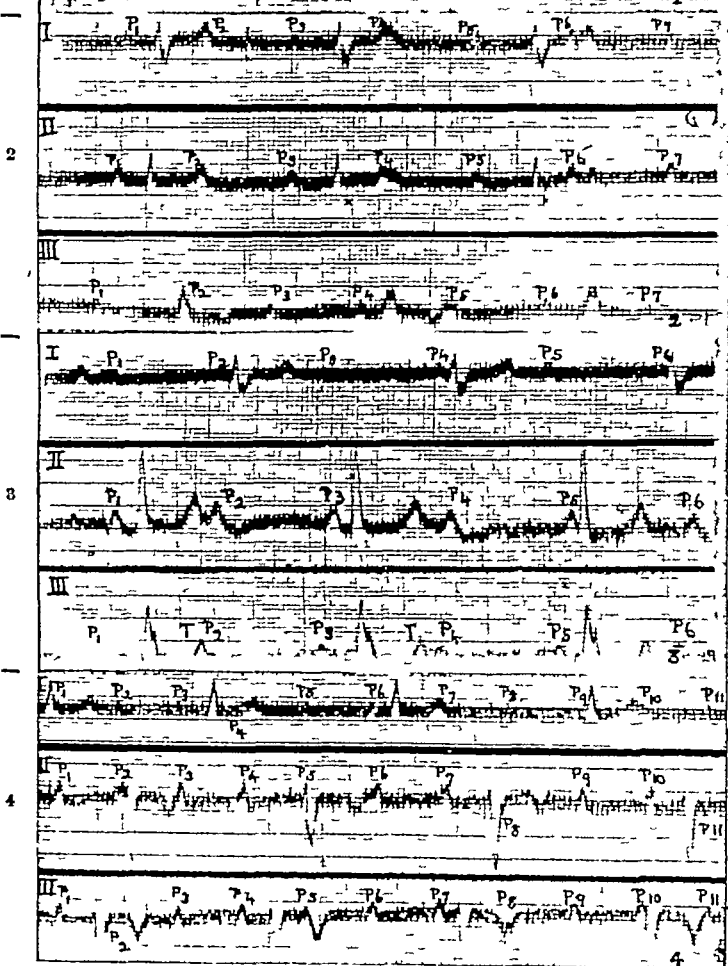


Fig 2 (Case 2) Leads I, II and III taken in 1935 showing complete heart block auricular rate 84 and ventricular rate 30 per minute P R P interval (P4-P5) in lead III is the only interval that showed shortening Right bundle branch block is present in addition

N.B.—Three abnormal waves marked (x) are seen one positive in LI between P2 and P3 and two negative in lead II, one immediately after R2 and the other after R3 Are they auricular premature contractions? and if so do the two negative P waves represent retrograde conduction? The second E.C.G. taken on the same day did not show these abnormal waves

Fig 3 (Case 3) Leads I, II and III taken in 1938, half an hour after an injection of 1/50 gr atropine P R P intervals (P1 P2) and (P3 P4) are shorter than P P intervals in lead II In lead III, at a glance, it looks as if P1 P2 is shorter than P2-P3, but when actual measurements are taken they are the same This is due to increase in acceleration of the plate Arborization block is seen in lead III in addition

Fig 4 (Case 3) Leads I II and III showing complete heart block auricular rate 120 per minute, ventricular rate 48 per minute Shortening of P R P intervals are due to retrograde auricular contractions P4 in lead I P8 and P11 in lead II, and P2 in lead III are retrograde conductions and all are negative Retrograde conduction time (R P) varied from 0.08 to 0.12 second

Except for the single shortening of the P-R-P interval (P4-P5) in lead III no abnormalities were noticed

A second ECG taken on the same day showed exactly similar findings

A third ECG taken four years later (1938) showed in lead II (Fig 3, Raman 1944) shortening of P2-R1-P3 interval as compared with the other P-P intervals. Actual measurements could not be given since the time marker was not working. The other two leads I and III did not show any change.

An injection of 1/50 gr of atropine sulphate showed the following changes

In the ECG (Fig 4, Raman 1944 loc cit) taken 15 minutes after atropine, P-P and P-R-P intervals were the same (0.92 seconds). P1 and P3 were fused with R in lead II and P2, P4 and P6 were fused with R in lead III.

TABLE 3 ECG (Fig 3)

Half an hour after atropine		P-P in seconds	P-R-P in seconds
Lead II	P1-P2		0.88
	P2-P3	0.92	
	P3-P4		0.88
	P4-P5	0.92	
	P5-P6		0.92

P-R-P was shorter than P-P interval only twice. There was no change in the other two leads. Retrograde conduction was absent.

Case 3—A case of myocarditis of unknown causation in a Hindu male aged 48 years.

TABLE 4 ECG (Fig 4)

		P-P in seconds	P-R-P in seconds	P-R and R-P in seconds	Remarks
Lead I	P1-P2	0.52			
	P2-P3	0.52			
	P3-P4		0.40	P3-R2 0.28	P4 negative showing retrograde conduction R-P = 0.10 second
	P4-P5	0.64		R2-P4 0.10	
	P5-P6	0.40		P6-R3 0.20	
	P6-P7		0.52	P9-R4 0.12	
	P7-P8	0.52			
	P9-P10		0.52		
	P10-P11	0.52			
Lead II	P1-P2	0.52		P2-R1 0.04	P5 and R2 are super imposed. P8 negative showing retrograde conduction R-P = 0.08 second. P11 negative showing retrograde conduction R-P = 0.12 second
	P2-P3		0.52	P7-R3 0.32	
	P3-P4	0.50		R3-P8 0.08	
	P4-P5		0.50	P10-R4 0.24	
	P5-P6	0.52		R4-P11 0.12	
	P6-P7	0.50			
	P7-P8		0.12		
	P8-P9	0.60			
	P9-P10	0.50			
	P10-P11		0.42		
Lead III	P1-P2		0.10	P1-R1 0.28	P2 negative showing retrograde conduction R-P = 0.08 second
	P2-P3	0.64		R1-P2 0.08	
	P3-P4	0.52		P4-R2 0.24	
	P4-P5		0.52	P7-R3 0.16	
	P5-P6	0.52		P10-R4 0.04	
	P6-P7	0.52			
	P7-P8		0.52		
	P8-P9	0.52			
	P9-P10	0.52			
	P10-P11		0.52		

Eleven P waves were seen in each of the three leads I, II and III. P-R-P interval was shorter (0.40 sec) once in lead I, twice in lead II (0.42 sec each) and once (0.40 sec) in lead III. Retrograde conduction was present once (P4) in lead I, twice in lead II (P8 and P11) and once in lead III (P2). In all these retrograde conduction P was negative. The R-P intervals varied from 0.08 to 0.12 second.

The retrograde auricular contractions in these cases were premature.

Lead I    P1-P2 + P2-P3 = 1.04 sec

          P3-P4 + P4-P5 = 1.04 sec

Lead II   P5-P6 + P6-P7 = 1.02 sec

          P7-P8 + P8-P9 = 1.02 sec

          P5-P6 + P6-P7 = 1.04 sec

Lead III   P1-P2 + P2-P3 = 1.04 sec

All the three leads showed a compensatory pause for the auricular contraction after the retrograde conduction.

Case 4—A case of syphilitic myocarditis in a Hindu male aged 50 years.

TABLE 5

		P-P	P-R-P
		in seconds	in seconds
Lead II	P1-P2		0.04
	P3-P3	0.04	
	P13-P14	0.04	
	P14-P15		0.04
	P18-P19	0.04	
	P19-P20		0.04

Since the intervals are the same the intervening figures are not given.

There was no difference between the P-P and P-R-P intervals. In another ECG lead II (Fig 6 Raman 1944 loc cit) showed ventricular extra-systoles in addition to complete heart block. The extra-systole occurred immediately after P4. There was no retrograde rhythm.

#### DISCUSSION

The irregular auricular contractions that occur in cases of complete heart block result in the decrease in P-R-P interval, (during which ventricular contractions intervene between two auricular contractions), as when compared with P-P interval, (during which ventricular contractions are absent), and this phenomenon has been explained in different ways by different authors. Winternitz and Langendorf (loc cit) have found this often in complete heart block and called it "ventriculophasic sinus arrhythmia in heart block".

In case (1) leads II and III showed that P-R-P intervals were shorter than P-P interval by 0.08 second on five occasions and by

0.12 second once. In case (2) shortening was observed only once and that too by 0.04 second in lead III. ECG taken four years later showed reduction of P-R-P interval only once in lead II. An injection of 1/50 gr of atropine sulph did not show any change in the interauricular interval after fifteen minutes, but the ECG taken after half an hour showed reduction of P-R-P interval twice by 0.04 second in lead II only. In case (3) shortening occurred once in lead I, twice in lead II, and once in lead III and all these were due to retrograde premature contractions. In case (4) there was no change in the intervals. P-P intervals were never smaller than the P-R-P intervals in any of the cases.

Erlanger and Blackman (1909) loc cit suggested that increase in the vagal tone increases the P-P interval which follows a ventricular contraction. Wenckebach and Winterberg (1927) suggested that changes in the blood supply of the sino-auricular node, i.e., stimulation during the systole and depression during the ventricular diastole, as the cause of the changes in the inter-auricular interval. Direct stimulation of the sino-auricular node by the contraction of the ventricle has been suggested as the third possible explanation of the phenomenon (Parsonnet and Miller loc cit).

The occasional increase of P-R-P over P-P interval and the absence of correlation between the R in the P-R-P interval and the succeeding P-P interval have not been fully explained. According to Parsonnet and Miller (loc cit) the inter-auricular period is controlled by two opposing forces: (1) The absence of ventricular contraction which increases the P-P interval and (2) the increase in intra-auricular tension which decreases the interval. In case (1) of the present series the shortening of the P-R-P interval was observed only in leads II and III but why it was not present in all the leads is not clear. Case (2) showed this only once and that too in lead III only. The decrease in P-R-P interval was observed in lead II half an hour after an injection of 1/50 gr of atropine sulph. The shortening in case (3) could be easily explained by the occurrence of retrograde auricular contraction.

Retrograde conduction was present in one case only. The ECG (Fig 4) showed clearly the retrograde rhythm in all the three leads, I, II and III. P was negative in all and R-P intervals varied from 0.08 to 0.12 second. The amplitudes of normal P's varied from 2 to 3 mms and the breadth from 0.04 to 0.08 second. Retrograde P's, P<sub>4</sub> (lead I), P<sub>8</sub> and P<sub>11</sub> (lead II) and P<sub>2</sub> (lead III) were small and the amplitude varied from 1 to 2 mms.

Winternitz and Langendorf (loc cit) from a critical study of twenty-five cases of complete and incomplete heart block observed that in retrograde conduction P was always negative in leads II and III but may be positive in lead I, and R-P interval varied from 0.1 to 0.23 second.

Kline et al (1939) observed that the shortest P-R interval that permitted the subsequent retrograde conduction was 0.32 second. Winternitz and Langendorf (*loc cit*) showed that the maximum auricular rate that permitted retrograde conduction was 120 per minute. In case (3) of the present series the auricular rate was 120 per minute and the minimum P-R that permitted subsequent retrograde conduction was 0.24 second and the maximum 0.32 second.

The mechanical theory of Wilson and Robinson (1918), the different pathway theory of Danieleopolu and Danulesco (1919) one for orthograde and another for retrograde conduction, and the supernormal recovery phase theory of Kline et al (1939) have all been found unsatisfactory by Winternitz and Langendorf and they have put in the hypothesis that both orthograde and retrograde conductions are only two different functions of the same conducting pathway.

#### SUMMARY

1 Ten electrocardiograms of four patients suffering from complete heart block were re-examined for evidence of shortening of P-R-P interval, and retrograde (V-A) conduction.

2 The literature of this condition has been reviewed.

3 Three cases showed decrease in the P-R-P interval and in no case was the P-P interval shorter than P-R-P.

4 Retrograde conduction was present in one case. P was negative in all the leads that showed this conduction, and the shortest P-R interval that permitted subsequent retrograde conduction was 0.24 second. R-P interval varied from 0.08 to 0.12 second.

5 The possible theories as to the causation are discussed.

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# MENINGITIS\*

## AN ANALYSIS OF 255 CASES

by

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Purulent meningitis has always been a medical emergency and with the exception of meningococcus meningitis the prognosis has been extremely poor even after the advent of sulphonamide therapy. Penicillin promises more hopes and the results are quite encouraging. The case mortality rate for those who developed acute purulent meningitis was over 90 per cent. The use of sulphonamide compounds and of penicillin has lowered the mortality rate appreciably but has not detracted from the emergency which exists, when a case of purulent meningitis is encountered.

It is proposed in this paper to study from clinical point of view, all the cases of purulent meningitis admitted to the K.E.M. Hospital, Bombay, during the period 1st January 1941 to 30th September, 1944. There were 255 cases of meningitis during this period and analysis of these cases is given below. These cases include those due to coccal infections viz, meningococcal, pneumococcal, streptococcal etc, those due to tuberculosis infections, those known as Benign Lymphocytic meningitis and those cases of purulent meningitis wherein no organisms could be seen in smear or culture. Cases of syphilitic basal meningitis and syphilitic meningitis have not been included in this list.

During three years and nine months, 255 cases of meningitis were admitted as in-patients in the K.E.M. Hospital, Bombay. During that period the total number of in-patients treated in the Hospital on the medical side was 21,567, so that meningitis cases formed 1.18 per cent of the total number of admissions on the medical side or in other words for every 85 cases admitted in the Hospital on medical side there was one case of meningitis. The yearly incidence of meningitis is shown in Table 1.

The incidence has remarkably increased during 1943 and 1944, more than double in 1944 as compared to percentage in the years 1941 and 1942. It is probably due to over-crowding and insanitary conditions resulting from it, that are responsible for the high incidence.

Table 1 Showing % incidence of meningitis to total admissions on medical side

Year	No. admitted on med. side.	Meningitis cases.	per cent of cases
1941	5,200	43	0.82
1942	5,155	87	0.72
1943	6,136	80	1.30
1944 up to Sept.	5,067	95	1.87
Total	21,567	255	1.18

\* A paper read at the 48th scientific meeting of G. S. Medical College and K. E. M. Hospital Staff Society, Bombay, on May 12, 1945, with Dr. N. D. Patel, M.D. (Lond.) in the chair.

*Age.*—The youngest age at which meningitis occurred in the present series was 6 months while the oldest case was 65 years old. The age incidence in various forms of meningitis is given in Table 2. Cases in which organisms have not been found in either smear or culture of C.S.F. and wherein there is polymorphonuclear pleocytosis have been put under the heading of unknown aetiology (?). These cases are mostly of meningococcal or pneumococcal meningitis.

Table 2 Age incidence in various forms of Meningitis

Age in Years	Meningo coccic.	Pneumo coccic.	?	T B	Benign Lympho-	Total	Per cent.
1-10	5	8	2	24	1	40	15.65
11-20	20	11	9	11	nil	51	20.00
21-30	35	20	18	17	1	91	35.70
31-40	7	15	8	8	1	39	15.31
41-50	4	16	1	5	nil	26	10.20
51-60	2	1	nil	nil	nil	3	1.18
61-70 above	1	2	2	nil	nil	5	1.96
Total	74	73	40	65	3	255	100.0

The maximum incidence of meningitis in the ten years group is 91 cases between 21-30 years on the whole. Over 25 per cent of cases of meningitis occurred in the first forty years of life. On plotting a curve of age incidence in meningitis, we find that the curve shows a steep rise between 21 and 30 years and a steep fall between the period 31 and 40 years and after that there is a gradual fall throughout.

The maximum and minimum ages in various forms of meningitis are shown below.

Table 3 Maximum and minimum ages in various forms of meningitis

Type of meningitis	Minimum age	Maximum age
Meningo	6 months	65 years
Pneumo	1 year	65 years
T B	1 year	50 years
Benign Lympho	8 years	40 years
Unknown	4 years	65 years

Majority of cases of T.B. meningitis occurred during first ten years of life. This is probably due to the fact that miliary tuberculosis is more common at this age than at any other. 24 out of 65 cases of T.B. meningitis in the present series occurred at this age. Even this figure is very low and is due to the fact that admissions of children in K.E.M. Hospital is very restricted and the neighbouring hospital for children might have accommodated many more cases of T.B. Meningitis.

*Sex Incidence.*—In the present series there is a definite preponderance of males over females. But these figures are taken from a hospital where there is a remarkable preponderance of male admissions and so these figures are compared to male and female admissions in the hospital on medical side in the following table.

Table 4

	Total	Male	Female	Male per cent.	Female per cent.
Cases of Meningitis	255	196	59	76.87	23.13
Total no admitted on med. side	21,507	17,055	4,452	79.08	20.92



From the above table, it is evident that incidence of meningitis is not higher in males than in females,—if at all, it is slightly higher in females than in males

The annual sex incidence is shown in Table 5 which shows that incidence in females is higher in the years 1941 and 1942 whereas that in males is higher in the year 1943

Table 5 Annual sex incidence.

Year	Total	Male	Female	Male per cent.	Female per cent.
1941	43	27	16	62 80	37 20
1942	37	25	12	67 57	32 43
1943	80	70	10	87 50	12 50
1944 up to Sept.	95	74	21	77 90	22 10
Total	255	196	59	76 87	23 13

*Community*—Here we find that there is a marked preponderance of meningitis amongst Hindus compared with others 195 out of 255 cases were in Hindus But the number of admissions of Hindus to K.E.M. Hospital far exceeds the number of admissions of the rest Comparing the percentage of meningitis cases in different communities with the percentage of their admissions, we find that the incidence is slightly more in Hindus and slightly less in Christians

Table 6.—Incidence of meningitis in different communities

COMMUNITY	Meningitis No of Cases	%	Total admissions in the hospital NUMBER	%
Hindus	195	76 47	36,896	69 34
Moslems	42	16 47	8,230	15 40
Christians	17	6 66	6,857	12 88
Others	1	0 40	1,228	2 32
Total	255	100 0	53,211	100 00

*Occupation*—Meningitis occurred in men having different types of occupation but most of the persons affected were either mill-hands or factory-hands, and coolies This is probably due to their poor economical conditions and unhygienic surrounding in which they lived that was responsible for the occurrence of meningitis It is known that meningitis is quite common amongst medical students and nurses In the present series not a single case occurred amongst them Out of 155 males, occupation was not known in 46 cases In the remaining the occupations were as follows —

Mill hands & Factory hands	44	Barbers	2
Coolies	10	Sweepers	2
Hotel servants	8	Motor mechanics	3
School students	6	Businessmen	2
Milk men	4	Farmers	2
Domestic servants	5	Watchmen	4
Blacksmiths & Carpenters	3	Clerks	2
		One case of each of Doctor Tailor, Pressman, Sadhu, Hawker, and Panwalla	
		Total	109

Table 7.—Yearly incidence of different types of meningitis

Year	Meningo	T.B	Pneumo	Benign Lympho.	Unknown	Total
1941	0	11	16	1	9	43
1942	5	14	13	nil	5	37
1943	35	18	19	nil	8	80
1944 up to Sept.	28	22	25	2	18	95
Total	74	65	73	3	40	255

The incidence of meningitis has remarkably increased in the year 1943 and 1944. This is mainly due to an increase of meningococcal meningitis, though tuberculous and pneumococcal meningitis have also a higher incidence during the same years. All this can be ascribed to overcrowding with all its bad effects that increased the incidence of pneumococcal and tuberculous infections in the body.

The incidence of meningitis depends upon several factors, such as incidence of tuberculosis in general, of otitis media, of influenza and upon the presence or absence of epidemics of meningococcal meningitis.

*Meningococcal Meningitis*—This is primary condition though naso-pharyngeal infection is often an exciting factor. Van Orden and Armentrout reported on 39 cases of meningococcal meningitis. 8 out of 39 cases gave a history of previous naso-pharyngeal infection. No mention was made about naso-pharyngeal infection in the present series of 74 cases of meningococcal meningitis. Out of 74 cases 3 cases occurred secondarily—2 cases occurred after head injury whereas one occurred after mastoiditis.

*Pneumococcal Meningitis*—Keefer divides pneumococcal meningitis into three groups: (1) Cases that follow pneumococcal pneumonia, (2) Those following infections of ears, mastoid or paranasal sinuses, and (3) Primary. Those in which the focus is undetermined.

The relative incidence of each group is given in Table 8. Out of the 31 cases occurring after pneumonia, one case developed empyema first and then meningitis.

Table 8

Exciting Factors	No. of cases	per cent
Pneumonia	31	43.40
After cataract operation	1	1.39
Ear, mastoid and sinuses	10	13.70
Head injury	6	8.20
Primary—No exciting factor	25	34.25
Total	73	100.00

Ear, mastoid and sinus infections were responsible for 17 cases of pneumococcal meningitis. Out of these 17 cases, otitis media and mastoid were to be blamed in 9 cases only. 6 cases of pneumococcal meningitis occurred after head injury leading to fracture base of skull. One case occurred after frontal sinus operation and a solitary case occurred after cataract operation. In 25 cases the focus was undetermined and they are put under the heading of Primary Pneumococcal meningitis.

In the present series of 255 cases of meningitis, head injury was responsible for 9 cases of meningitis. Out of these 9 cases, 6 cases were pneumococcal, 2 cases were meningococcal, and one case did not show the presence of any organisms in smear or culture examination.

Otitis media and mastoiditis lead to meningitis in 11 cases in this series of 255 cases. Out of these 11 cases, 8 cases were pneumococcal, 1 case was meningococcal, and 2 cases did not show the presence of any organisms in smear or culture-examination.

**Tuberculous Meningitis**—Any disease which lowers the patient's resistance may precipitate tuberculous meningitis in a patient previously infected with tubercle bacilli. Measles and pertussis are often fore-runners of tuberculous meningitis. Trauma and operations also act in the same way. In this series, no mention was made about measles and pertussis. Out of 65 cases of T.B. meningitis, 21 cases had some tuberculous focus elsewhere in the body, whereas in the remaining 44 cases, no focus was detected and these are grouped as primary cases. Table 9 shows the details of the primary foci in cases of secondary meningitis.

Table 9

Exciting Factor	No. of cases	Per centage
Primary—no exciting factor	44	67.70
SECONDARY	21	32.30
Pulm. T. B.	11	52.38
Adenitis	7	33.33
Osteomyelitis	2	9.52
Tuberculoma	1	4.76
T. B. Abdomen	1	4.76
Fistula in ano	1	4.76
After operation for chr. metritis	1	4.76
After abortion	1	4.76
Total	65	100

2 bone cases were put in plaster of Paris—one case of T.B. spine and the other of T.B. ankle, and subsequently they developed meningitis.

1 case occurred after operation—Hysterectomy was done on a case of chronic metritis.

1 case developed meningitis following an abortion.

In the above Table, 3 cases had both pulmonary and glandular tuberculosis and one case had both pulmonary tuberculosis and T.B. fistula-in-ano.

**Clinical Features**—The symptoms of meningitis are very suggestive and occur with a fair amount of constancy, which justifies our suspecting the presence of meningitis from the history alone, and very often guide us to make a fairly accurate diagnosis from clinical examination. Headache is the most common and earliest symptom of meningitis regardless of cause. The headache of meningitis is often intense and agonising. The onset is usually sudden with malaise, high or gradually rising fever and stiffness of the neck—slight at first, increasing as the disease progresses, and often causing re-

traction of the neck Other symptoms are vomiting, convulsions, involuntary movements, paralysis, photophobia and hyperaesthesia The relative constancy with which they occurred is shown in the following table

Table 10 Relative frequency of symptoms in meningitis

Symptoms	No of cases	Percentage
Fever	240	94.1
Headache	75	29.4
Convulsions and involuntary movements	40	15.7
Vomiting	30	11.8
Paralysis	13	5.1
Photophobia	10	3.9
Hyperaesthesia	7	2.7
Total	255	100.0

Fever was not present in 15 cases who were admitted in a gasping condition with severe collapse and in others the disease was so severe that there could be no body response of the nature of fever

*Headache*—About 131 cases were not able to give history because they were admitted in an unconscious condition with definite evidence of meningitis and so no attempt was made to get the history from relatives 29 were children under the age of 5 years and proper history was not available in them Out of the remaining 95 cases, headache was present in 75 cases

Involuntary movements were present in 15.7 per cent of cases These movements were choreic, athetoid or irregular movements of the extremities or twitchings and spasms of the muscles In 2 cases, there were typical pill rolling movements like those seen in parkinsonism Out of 40 cases with involuntary movements 24 cases got generalised convulsions, epileptiform in nature Out of these 40 cases 14 cases were pneumococcal 15 cases were tuberculous, 6 cases meningococcal and 5 cases of (?) meningitis Involuntary movements are due to cerebral irritation, and occur at an advanced stage of the disease and have therefore a bad prognostic significance

Paralysis apart from that of cranial nerves was observed in 13 cases as shown below

Hemiplegia 7 cases  
 Monoplegia 1 case.  
 Aphasia: 5 cases

Whether the paralysis is transient or it remains for a variable period after the patient is cured of meningitis, is difficult to say Out of these 13 cases, 6 cases were of T B meningitis, 3 cases of meningococcal, 2 cases pneumococcal meningitis and 2 cases of (?) meningitis Excepting for 2 cases of meningococcal meningitis that were transferred to Arthur Road Hospital, all cases expired in K.E.M Hospital

*Hyperaesthesia*—It is important to remember this symptom because it might predominate the clinical picture of meningitis 2 cases were admitted as cases of polyneuritis and lumbar puncture was done to get cerebro-spinal fluid examined for routine and Wasser-

mann reaction in cases of acute polyneuritis, and this revealed the true nature of the disease. Hyperaesthesia is more common with acute than with chronic meningitis. In the present series, hyperaesthesia was present in 7 cases (27 per cent). 5 cases were meningococcal, one case of pneumococcal, and one case of (?) meningitis.

**Signs**—There are definite signs by which meningitis can be diagnosed clinically. Rigidity of neck was present in 201 cases whereas Kernig's sign could be elicited in 179 cases. 179 cases developed unconsciousness. Out of these 179 cases, 131 were admitted in an unconscious condition and so they could be diagnosed easily.

Pupillary changes were present in 83 cases. The most important pupillary abnormalities found were dilated pupils, not reacting, or reacting very sluggishly to light. Other abnormalities found were unequal pupils or small pupils not reacting to light.

Slow pulse 60 or less per minute was present in 27 cases, and is due to an increased intracranial pressure.

Cranial nerve palsy was present in 20 cases and some of these were admitted as cases of syphilitic basal meningitis. As the sixth nerve is the longest cranial nerve, it is very easily affected. Out of 20 cases of cranial nerve palsy, 10 cases were of sixth nerve palsy alone. Other nerves affected were as follows:

- 6 Cases of VII nerve palsy
- 2 Cases of III nerve palsy
- 1 Case of III, IV and VI nerve palsy
- 1 Case of III and VII nerve palsy

The different types of meningitis responsible for clinical nerve palsy were as follows:

Table 11 Cranial nerve palsy in various types of meningitis

Type of Meningitis	No. of Cases.
Tuberculous	8 cases of VI 2 cases of III 2 cases of VII 1 case of III, IV, & VI
Pneumococcal	4 cases
Meningococcal	4 cases
Of unknown aetiology (?)	4 cases
Total number of cases	20

Out of these 20 cases, 3 recovered. One case was a meningococcal case of VII nerve palsy. Facial paralysis was present when the patient was discharged after about ten weeks, in spite of treatment with large doses of vitamin B1. As the case was not seen afterwards, we do not know what ultimately happened to that nerve palsy. The other two cases were of (?) meningitis. One had VI nerve palsy, and the other with the III and VII nerve palsy. This second case recovered very rapidly from cranial nerve palsy as he recovered from meningitis. Fundi were examined in 8 cases. 4 cases did not show any change. The remaining 4 cases showed the following changes:

- 2 cases showed secondary Optic atrophy
- 1 case showed Optic neuritis
- 1 case showed engorged veins

All these 8 cases were of tuberculous meningitis but in none of them, choroid tubercle was seen

Rash was observed in only 6 cases 5 cases were of meningococcal and one of tuberculous meningitis This case was given sulphapyridine and the rash appeared seven days after the drug was stopped

Rash in all these cases was haemorrhagic in nature with petechiae on the front of the body and the extremities

**Bulging Fontanelle**—Out of 255 cases, 13 cases were under the age of 2 years Bulging fontanelle was seen in 7 out of 13 cases 6 cases were tuberculous whereas one case was meningococcal in origin The details of clinical signs and their percentage occurrence is shown in the following table

TABLE 12 —Incidence of physical signs in meningitis

Physical Signs:	No of cases	Percentage
Rigid neck	201	78.8
Kernig's sign	179	70.2
Unconscious	170	70.2
Pupillary changes	83	32.5
Slow pulse	27	10.5
Cranial nerve palsy	20	7.8
Abnormal fundi	4	
Rash	6	2.3
Bulging fontanelle	7	
Herpes	2	0.78
Total no. of cases	255	100.00

Herpes febrilis was seen in 2 cases of meningococcal meningitis and both these cases recovered completely

On account of the varied clinical picture, the following cases were diagnosed wrongly

5 Cases were admitted as Tetanus: 4 of Meningococci, 1 of Pneumococci  
 2 Cases were admitted as Polyneuritis 1 of Meningo  
 1 of Pneumo  
 1 case was admitted as Intestinal obstruction—T. B.  
 2 Cases as Syphilitic basal meningitis 1 of T. B.  
 1 of Meningo,  
 1 Case as congestive cardiac failure Temperature of this case was normal Post mortem revealed  
 Otitis media with Pneumococcal meningitis in addition to Congestive cardiac failure  
 2 cases were admitted in a collapsed condition as cases of some poisoning Post mortem revealed  
 meningitis—one of pneumococcal and the other of meningococcal meningitis.

**Investigations.**—Cerebrospinal fluid was examined in 244 cases the remaining 11 cases were diagnosed post-mortem These cases were the following

7 of pneumo—6 cases treated as pneumonia and one as congestive cardiac failure,  
 2 of T. B. — both treated as pulmonary T. B.  
 1 of meningo—treated as poisoning  
 1 of (?) — treated as fracture base of the skull

**Pneumococcal Meningitis**—Out of 73 cases, C.S.F. was examined in 66 cases and was found characteristic of purulent meningitis

Turbid fluid, increased proteins and globulin, diminished or absent sugar Pneumococci were seen in smears of 60 cases The remaining 6 cases with smear negative were stamped as pneumococcal meningitis on the following bases

2 cases had smear positive on post mortem  
 2 cases had positive culture  
 2 cases had typical lobar pneumonia with meningitis

Pleocytosis in C.S.F. varied from 11 cells to innumerable cells per cmm of C.S.F. with predominating polymorphs

In the present series, there was one case which showed the earliest evidence of meningitis. This case was treated for pneumonia—C.S.F. showed normal amount of protein, globulin, and sugar with 11 cells per cmm of C.S.F.—lymphocytes predominating. Smear showed the presence of gram positive diplococci. Blood and C.S.F. culture were negative. This case recovered with sulphapyridine, initial dosage being 4 tabs and then 2 tabs four times a day. 60 tabs were used in all in 11 days.

C.S.F. culture was done in 31 cases with positive result in 24 cases. Blood culture was positive in 4 cases and negative in 2 cases.

*Tuberculous Meningitis*—Out of 65 cases of T.B. meningitis, C.S.F. was examined in 63 cases, 2 cases were diagnosed post mortem. C.S.F. in these cases was hazy or slightly turbid with cob-web formation on standing. There was increased amount of proteins, and globulin, with diminished sugar. Pleocytosis varied from 14 to 2614 cells per cmm of C.S.F. lymphocytes predominating. Tubercle bacilli were detected either in the cob-web or the smear by concentration method in 11 cases.

Estimation of chlorides is of great diagnostic value. It is believed that clinical picture of meningitis with markedly diminished chlorides below 580 mgms per 100 cc of C.S.F. is pathognomonic of T.B. meningitis. In other types of purulent meningitis, it is often reduced, about 650 to 680 mgms per 100 cc of C.S.F.

In this connection, I want to refer a case of Hindu male, aged 20 years admitted with a clinical picture of meningitis. History of headache and fever of 8 weeks' duration. Fundi showed bilateral secondary optic atrophy. C.S.F. showed Turbid fluid 1,818 cells per cmm lymphocytes, proteins 0.5 per cent. Increased globulin. Sugar Absent. Bacteria Nil, No growth or culture. Wassermann reaction was negative. Blood Kahn Negative. C.S.F. Chlorides 559 mgms present. Lange's Colloidal Gold reaction showed meningitic curve.

He went home against medical advice after staying for 62 days in the hospital. Clinically he improved remarkably—headache had disappeared, fever had subsided, and C.S.F. showed clear fluid, 38 cells, lymphocytes, and polymorphs in equal number. Protein 0.5 per cent. Globulin Increased. Sugar Absent. Bacteria Nil. I do not know the cause of this chronic meningitis.

*Meningococcal Meningitis*—Out of 75 cases C.S.F. was examined in 73 cases. Appearance of fluid varied from slight haziness to frank turbidity. Proteins 0.5 per cent. Globulin Increased. Sugar Absent or diminished. Pleocytosis, polymorphonuclear in nature varied from 177 cells to 68,266 cells cmm of C.S.F. Meningococci were seen in smears in 65 cases. In this connection I want to refer 2 cases of meningitis with smears of C.S.F. showing the presence of gram positive cocci. In one case, meningococci were grown in culture whereas in the other, post mortem diagnosis turned out to be meningococcal.

coccal meningitis CSF culture reports were available of 34 cases with positive culture in 23 cases and negative in the remaining 11 cases Chloride estimation was carried out in 6 cases The minimum figure recorded was 486 mgms per cent This case is atypical in the chlorides content as such marked reduction of chlorides occurs only in T.B meningitis The maximum figure recorded was 693 mgms of chlorides per cent

Blood culture was done in 2 cases with negative results in both *Meningitis of Unknown aetiology* CSF was examined in 39 cases out of 40 cases One case was fracture base of the skull which developed meningitis, post-mortem also did not show the presence of any organisms CSF in all these cases was turbid, with increased protein and globulin, with diminished or absent sugar, pleocytosis, polymorphonuclear in nature and absence of any organisms in either smear or culture

*Benign Lymphocytic Meningitis*—3 cases have been recorded under this heading, because all the three cases recovered completely They had lymphocytic pleocytosis in their CSF which was turbid with increased proteins and globulin, (protein 0.2 to 0.5 per cent) pleocytosis varied from 220 to 1060 cells per c.mm of CSF, sugar was absent in 2 cases and was normal in the 3rd case Chlorides were 668 mgms, 660 mgms and 577 mgms No bacteria were seen in smears or grown in culture Wassermann reaction was negative All these three cases recovered completely and were discharged in about two to three weeks Symptomatic treatment was carried out in all cases, with sulphapyridine 9 tabs and 24 tabs in two cases Though these cases are stamped as benign lymphocytic meningitis they are very atypical, because in 2 cases sugar in csf was absent and in the 3rd case, chlorides were markedly diminished in CSF—577 mgms per 100 c.c In benign lymphocytic meningitis, sugar content of CSF is usually within normal limits and chloride content in this disease is about 700 mgms per 100 c.c, though in an exceptional case recorded by Allen and Spencer, the chloride content attained surprisingly low figure of 500 mgms per 100 c.c

*Blood Kahn*—This was tested in 15 cases, out of which it was negative in 12 cases and positive in 3 cases

*C.S.F. Wassermann*—This was carried out in 20 cases In six cases it was strongly positive In 6 cases it was anti-complementary, and in 8 cases it was negative

Out of total 8 cases with positive Kahn and Wassermann, (3 cases of Kahn positive and 6 cases of W.R positive) one had both Kahn and W.R positive, 5 cases were of (?) meningitis, 2 cases of meningo and one case of pneumococcal meningitis

It is very difficult to draw any conclusion from these syphilitic cases Question often arises whether they are more susceptible to meningitis as a result of devitalisation of their nervous system by the spirochaete One case was treated for pneumonia and he developed slight rigidity of neck Lumbar puncture showed nothing abnormal excepting for positive W.R subsequently he developed pneumococcal



meningitis Here again one doubts as to whether first lumbar puncture could be responsible for the precipitation of meningitis—lowering of tension of C.S.F. by lumbar puncture might have allowed the passage of pneumococci from blood into C.S.F. and affected the brain which was already devitalised by neuro-syphilis No definite opinion can be given over this

#### TREATMENT

In addition to symptomatic treatment, all cases of purulent meningitis were treated with chemotherapy Serum was not used in any of these cases in the present series Penicillin was not available during this period

*Meningococcal Meningitis*—Out of total 74 cases, 37 cases were treated in K.E.M. Hospital with varying dose of sulphonamide group of drugs Sulfanilamide, sulphapyridine, sulphathiazole, sulphadiazine and sulphamerazine were used

19 cases that recovered from this treatment, were treated as follows —

1 case with sulphamerazine—42 tabs in 4 days

18 cases were treated with sulphapyridine—1684 tabs

Inj Sodium Sulphapyridine—22 gms

Inj Soluseptasine—130 c c

Out of these 18 cases, 2 were children of 5 and 10 years of age, for whom 30 and 38 tabs of M & B 693 were given respectively, and the latter was also given 1 gm of soluble sodium daganan Thus 16 adults were treated and cured by using the following —

1616 tablets of sulphapyridine

21 gms of inj sodium sulphapyridine

130 c c of inj soluseptasine

The remaining 15 cases that were treated at K.E.M. Hospital in the same way expired—5 cases died within 24 hours of their admission to the hospital

3 cases were treated symptomatically and they expired in the hospital They were not diagnosed during life

#### *Pneumococcal Meningitis*

"Although it has been said by some that the mortality rate since the advent of sulphonamide compounds has been about 35 per cent, unfortunately, it has been our experience that this is entirely too low, and that the mortality rate in cases of pneumococcal meningitis is nearer 85 per cent" This is said by Alison H Price, but we are more unfortunate than that Out of 73 cases of pneumococcal meningitis, only 4 cases recovered In none of these 4 cases, pneumococci could be grown from the C.S.F. They were all male patients between 12 and 32 years 61 cases were treated with sulphonamide group of drugs—4 cured and 57 expired

One case was admitted for pneumonia He developed empyema and subsequently meningitis In empyema fluid, pneumococci were

seen in smears and were also grown on culture media CSF showed the evidences of purulent meningitis with 215 cells—polymorphs, and pneumococci were seen in smears but could not be grown on culture media—probably because he was already being treated with sulpho-  
namide group of drugs This case was treated with sulfanilamide 44—128 tabs Inj sulfanilamide 44—80 cc and M & B 693—94 tabs—all these were used up in fourteen days CSF was normal when the patient was discharged

Second case was of pneumonia with clinical picture of meningitis CSF showed the following—

Proteins	Normal
Globulin	,
Sugar	
Cells	11/c mm Lymphocytes
Bacteria	Gram positive diplococci seen
Culture	No growth
Blood culture	No growth

This case is a very early case of pneumococcal meningitis and was treated successfully with M & B 693 tabs 60 tabs were given in 11 days

The third case was a male, 24 years old, with typical meningitis with CSF showing the following—

Appearance	Turbid
Proteins	0.5%
Globulin	Increased
Sugar	Absent
Cells	25,600/c.mm Polymorphs
Bacteria	Gram positive diplococci seen

He was cured by giving M & B 693 tabs 40 tabs and 2 gm of inj sodium daganan This was a very advanced case and was surprisingly cured by relatively a very small dose of sulphapyridine Unfortunately pneumococci were not typed in any of the cases of the present series and so we do not know the virulence of the organisms in any particular case

The fourth case was a male of 32 years, who had all signs of meningitis with the CSF showing the following changes Turbid fluid, with increased proteins and globulins, and absence of sugar. Cells 5376—Polymorphs Pneumococci were seen in smears No growth on culture—He was given M & B 693, 107 tabs and inj dogenan 5 gms and injection soluseptasine 25 cc in the first 9 days after admission After that the treatment with these drugs was stopped even in spite of pyrexia persisting Temperature became normal 3 days after stopping the drugs, and the patient completely recovered

In all these 4 cases, we observe that they were treated with relatively small dose of sulphonamide group of drugs 2 cases out of these 4 cases, were advanced cases with 25,600, and 5,376 cells cmm and yet it is very surprising that such small dose was used

Whenever inj soluseptasine was used it was given intrathecally after removing the CSF It is the impression that by using soluseptasine in this way, CSF became clear very rapidly

As against the above 4 cases, we have got some cases in whom early diagnosis was made and intensive treatment was given and yet they became progressively worse and expired In some of these

C.S.F. was definitely getting clearer but the general condition became worse and nothing helped them. The following cases are worth recording.

**Case 1**—Male aged 25 years was admitted for lobar pneumonia and was treated with cibazol tablets, 69 tabs were given in 6 days. Temperature became normal and he was well for three days. On the fourth day, he developed fever, headache, with slight rigidity of neck. Lumbar puncture was performed within few hours of onset of these symptoms and C.S.F. showed turbid fluid 469 cells—mainly polymorphs, protein 0.2 per cent, increased globulin, absent sugar and pneumococci were seen in smears and were also grown in culture.

Patient was put on heavy dosage of sulphapyridine—32 tabs of M & B 693, 2 gms of soluble sodium daganan and 5 c.c. of soluseptasine intrathecally per day. Patient became normal on the third day and remained so for 5 days. All the signs and symptoms reappeared in spite of continuing the same heavy dose and he expired in 15 days. He was given 412 tabs of sulphapyridine, 14 gms of soluble sodium daganan, 55 c.c. of injection soluseptasine and one blood transfusion.

**Case 2**—Male aged 27 years got pneumococcal meningitis after an attack of otitis media, of 4 days' duration. C.S.F. showed turbid fluid, 1200 cells—polymorph, Proteins 0.4 per cent. Increased globulin and absent sugar. Pneumococci were seen in smears and grown in culture. Pneumococci were also grown from blood culture. He was put on soluble daganan intravenously 1 gm every 4 hours, and 4 tabs of M & B 693 by stomach tube every 4 hours. In addition one blood transfusion was given. He expired 3 days after the admission. He was given

Sulphapyridine 92 tabs  
Inj sodium daganan 19 gms  
Inj soluseptasine 30 c.c.  
One blood transfusion

**Case 3**—Male aged 30 years was treated for pneumonia by M & B 693. Patient got headache and vomiting. Lumbar puncture was done and nothing abnormal was found in the fluid. Fever persisted and rigidity of the neck became marked. Lumbar puncture was repeated after 3 days of the first one and it showed turbid fluid, with 7,168 cell polymorphs, proteins 0.4 gms increased globulin and absence of sugar. Pneumococci were seen in smears and grown on culture. Blood culture was also positive.

Blood Kahn Strongly positive  
C.S.F.W.R. Strongly positive

He was treated with the heavy dose of sulphapyridine both by mouth and intravenously as in the above cases. In addition anti-syphilitic treatment and two blood transfusions were given but nothing helped him and he expired in the hospital.

Meningitis of unknown aetiology were treated in the same way and the results are given below.

Table 13 Results in different types of meningitis

Type of meningitis	Cured	Expired	Otherwise	Total
Meningo	10	18 5 expired within 24 hours	87	74
T. B.	nil	57	12	67
Pneumo	4	63	4	73
Benign lympho	3	nil	nil	3
(*) Meningitis	14	20	0	40
Total	40	150	50	255

Table 14 Results according to treatment

	60 cases of pneumococcal meningitis		37 cases of Meningo coccus		34 cases of Meningitis of unknown etiology	
	Cured	Exp	Cured	Exp	Cured	Expired
Sulphonamide	4	57	10	13	14	16
Symptomatic	nil	8	nil	3	nil	4
Total	4	63	10	18	14	20

## DISCUSSION

Dr M J Shah discussed the importance of some symptoms like rash, arthritis, headache in the diagnosis of meningitis. Cranial palsy may be associated with not only tubercular meningitis but also in pneumococcal meningitis. He made an observation that sulpha drugs temporarily helps cases of tubercular meningitis. In his opinion, lumbar puncture should be done frequently in cases of meningitis treated with sulpha group of drugs.

Dr N K Sahar in reply to Dr Shah said meningitis is a septicaemia and inflammation of meninges is a part of the picture. Rash, arthritis and headache are due to septicaemia rather than due to meningitis. He found the prognosis of cases of meningitis not associated with septicaemia better than those with septicaemia. He mentioned that lumbar puncture was done only 4 times in the tetanus wards and all the four times the cases were not tetanus. Mistaken diagnosis of tetanus may have been made because of the history of stiffness of the body and convulsion. Delirium is associated with headache in cases of meningitis as opposed to typhoid where delirium follows the headache. This symptom has not been brought out in this paper. He thought that recovery of cases of tuberculous meningitis is unknown even though some claims have been made in this respect. Diminution of chlorides in CSF as the disease progresses is diagnostic of tuberculous meningitis.

Dr N D Patel asked whether in some cases quoted by the author as tuberculous meningitis, the CSF examination was repeatedly done. In his opinion this examination should be done frequently.

He also asked why organism like streptococcus, staphylococcus and influenza bacillus were not found in this series of cases

**Dr P Raghavan** emphasised the question put forward by Dr N D Patel. He mentioned the varying excretion of the various members of sulpha group of drugs in CSF sulphamerazine having the highest excretion. He emphasised the need for the simultaneous estimation of level of the drug in blood and CSF to have a check on the progress and the treatment of the case. He doubted the recovery in cases of tuberculous meningitis and suggested newer methods of diagnosis such as culture before the results could be relied upon.

**Dr A Hameed** quoted six cases of meningitis having a common picture, besides the symptom of meningitis. CSF examination showed everything normal except the turbidity and pleocytosis where polymorphonuclear cells predominated. Repeated cultures were negative. In one case blood culture was negative. These cases recovered with treatment by sulphapyridine administered in usual doses for 2 days. He enquired as to the etiology of these cases.

**Dr P K Sen** enquired whether there was any reason for the diminution of chlorides in these cases of tuberculous meningitis. He also wanted to know the incidence of sequelae like hydrocephalus and psychosis. He quoted two cases of meningitis with the only initial symptom of retention of urine which were treated in the surgical wards of the hospital for some time before the disease was diagnosed.

**Dr A K Talwalkar** said that two cases of tuberculosis of the spine developed headache, vomiting, optic neuritis and convulsions but no rigidity. Both had recovered and so far there were no symptoms. He was of the opinion that these were cases of tuberculoma rather than of meningitis.

**Dr N D Patel** in summing up said that this paper showed that material for clinical work at our disposal was large and congratulated Dr J K Mehta on bringing out this study of 255 cases. He cited few difficulties like inadequacies of notes, which for some reason or the other were always incomplete. There was also an inadequate examination of the patients. He gave an example of absence of examination of fundus of these cases of meningitis. He suggested that in this hospital besides aiming at the alleviation of suffering there should also be an academic study and that it could only be done by thorough examination and investigation of cases. He further said that in his practice he did not find any cases of tuberculous meningitis which had recovered. He was of the opinion that those cases which might have recovered may have been due to helminthic irritation, these cases often produced changes in CSF similar to those of tuberculous meningitis. The results of the treatment of meningococcal meningitis all over the world were good. The recovery rate in this hospital did not appear to be very complimentary.

# The Indian Physician

VOL IV NO 8

AUGUST 1945

WHOLE NO 44

## Original Contributions

### AMOEBIASIS IN CHILDREN

A BRIEF NOTE ON ITS INCIDENCE, WITH A REPORT OF A CASE  
OF AMOEBIC DYSENTERY IN A CHILD FOUR AND  
A HALF MONTHS OLD

by

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Amoebic dysentery has been considered to be rare in children and it is usual for the clinician to treat dysenteric states in children as bacillary dysentery. Gharpure and Saldanha (1931) in analysing the data from autopsy material at the Grant Medical College, Bombay, found the incidence of amoebic ulceration of the bowel in children under ten years of age, to be 0.9 per cent of all cases of amoebic colitis. There was no case of abscess of the liver in children of that age group in that series. These figures are not in agreement with those from elsewhere. Perry and Bensted from Egypt (1929) reported 73 instances of *End histolytica* infection in 526 examinations of stools of infants and young children and in another 12 instances in the series combined *End histolytica* and *Bac dysenteriae* was found.

Biggan (1932) in a letter to the editor of the *Lancet* emphasises the frequency of amoebic dysentery in children in Egypt and mentions the occurrence of amoebic colitis with abscess of liver in a child 3 months old. Beltram and Raul Larenas (1944) from Mexico reported a general parasitic infestation in 4 per cent of children between 0 to 6 months of age, 13 per cent in children between 7 to 12 months of age and 33 per cent in children, between 13 months and 2 years of age. The incidence of amoebiasis was found to be 0.3 per cent, 0.5 per cent and 2.0 per cent respectively.

The case reported here, was considered of interest because of the age of the child. The infection in this instance could be traced to the mother who was handling the feeding bottles of the child.

**Case Report**—Baby F, female, age 4½ months, was seen for frequency of stools. The mother had an attack of amoebic dysentery during the eighth month of gestation. A few hours after the birth of the child the mother had an eclamptic seizure from which she recovered with appropriate treatment. Because of this, the child was weaned from the birth and fed on humanised buffalo's milk. The

A paper read at the 40th Meeting of the G. S. Medical College and K. E. M. Hospital Staff Society, Bombay, on June 9, 1945, with Dr. V. R. Khanolkar, M.D. (Lond.) in the chair.

mother was handling the feeding of the baby. There was no history of gastro-intestinal upsets in the child at any time previously. The child on examination had a temperature of 102°F. The stools showed few pus cells and occasional red blood cells. The child was put on sulphaguanidine, the fever subsided and the frequency diminished considerably. After four days the child was still having 4 to 5 stools a day which were semi-solid and contained a fair amount of mucus.

The child was put on astringent mixture containing bismuth, pancreatin and takadiastase. At the end of the week the child still had frequency of stools associated with considerable discomfort during defaecation. The stools on examination showed vegetative forms of *Endamoeba histolytica*. The child was given subcutaneous injection of 1/8 grain of emetine once daily till she had a total dosage of 1 grain and 1/3 of a tablet of enterovioform thrice daily for five days. The stools examined subsequently two days after the course of emetine was finished, did not show any vegetative or cystic forms of *End. histolytica*. The child seen lately had no recurrence of the diarrhoea and was progressing normally.

#### COMMENT

It is necessary to bear in mind the possibility of amoebic infection in infants with frequency of stools and look for confirmation by repeated examinations of the stools, and then treat them adequately. Amoebic dysentery does not seem to be so uncommon in children as it is considered to be, and it is worthwhile investigating the incidence of the condition here.

Regarding treatment Teitel (1929) considered emetine to be the best drug in controlling amoebic dysentery in infants and children. It may be used alone or in combination with Rivanol or Yatren enemas. The dosage of emetine that has been suggested (De Langen and Luchtenstien) is 2.5 mg (grain 1/25) per day for every year of the child's age.

#### SUMMARY

(1) A brief review of the available literature on incidence of amoebiasis in infants and children is given. (2) A case of amoebic dysentery in a child 4½ months old is reported.

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# BRONCHOGENIC CARCINOMA

## A REVIEW OF THE LITERATURE WITH A REPORT OF EIGHT ILLUSTRATIVE CASES

by

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New growths of the lung have for a long time been supposed to be clinical curiosities and even in the autopsy room they created a sensation, and this was particularly so for the malignant neoplasms. This state of affairs was due to the mistaken notion of the rarity of pulmonary malignant neoplasms. With an awakening of the medical profession to the danger of malignant diseases in various parts of the body and more so with the recent advances in surgery and radio-therapy which have drawn a silver lining to the dark clouds of despair and which have inspired new hopes and longings in the hearts of the afflicted and the healer, there are indications that this mistake is being rectified surely though slowly.

It is proposed first to present the eight illustrative cases and then proceed to review the literature. It must be made clear to start with, that these are not the only cases of bronchogenic carcinoma that have been admitted in the K.E.M Hospital. No attempt has been made to derive any statistical evidence from this small series or from all the cases admitted in the K.E.M Hospital because it appears that the total number of cases is too small to be of any benefit from that point of view. These eight cases have been selected because each one of them represents a different type of clinical picture.

Case 1—Y R, a Deccani female aged 40, was admitted for multiple swellings all over the body and difficulty in breathing. Six months prior to admission she felt slight pain in the right mammary region and developed a dry unproductive cough which was more troublesome at night and on lying down flat. Two months later she felt breathless towards the evenings and the cough became more troublesome and paroxysmal in type. She carried on in this fashion for three more months with little relief. A month before admission she developed a small swelling in the right pectoral region, low irregular fever and completely lost her appetite. No family history of tuberculosis could be obtained.

On examination the patient was found to have six subcutaneous nodules varying from  $\frac{1}{2}$  to 1 inch in diameter. The skin over all, except one in the right pectoral region was free and normal. On the particular nodule in question the patient had applied some indigenous oil for a few days and the skin over it was warm, red, shiny and adherent to the nodule, which was softening in the centre. The nails were pale but there was no clubbing. The teeth were septic. The right side of the thorax showed very slight respiratory excursions and was absolutely dull on percussion upto the level of the third rib.

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A paper read at the 40th Meeting of the G. S. Med. College and K. E. M. Hospital Staff Society, Bombay, on June 9 1945, with Dr V. R. Khanolkar in the chair.



anteriorly The level of the dullness was not higher in the axilla Breath sounds were absent Above the area of dullness, there was harsh breathing with coarse rales during inspiration as well as expiration The left side of the chest was normal There was no engorgement of veins in the neck The right border of the heart could not be defined due to continuation of dullness all over the right side of the chest The apex beat was in the fifth left intercostal space  $4\frac{1}{2}$  inches away from the mid-sternal line The heart sounds were normal B P 110/70 mm of mercury The pulse was regular and 90 per minute at rest in bed There were no glands in the axilla or the neck Liver and spleen were not palpable There was a small nodule in the left lobe of the thyroid gland A diagnostic aspiration of the right pleural cavity was carried out and only about 50 cc of blood stained fluid could be drawn out RBC 35 million/c mm, Hb 54 per cent, C Index 0.77, WBC 28,000/c mm, P 75 per



Fig 1 —Case 1 (Dr N D Patel's case)

cent E nil, B nil, L 25 per cent, L M nil, Kahn test —ve Sputum—no elastic fibres, no malignant cells, no tubercle bacilli seen Screening of chest—Dense opacity on the right side upto the 2nd rib Right phrenico-costal sinus was obliterated, movements of the right dome of the diaphragm were not seen The mediastinum was pushed to the left by about  $\frac{1}{2}$  inch

Pleural fluid—Haemorrhagic—malignant cells could not be seen Section report of a subcutaneous nodule showed evidence of anaplastic carcinoma but there was no suggestion of a secondary from the thyroid gland

While under observation the patient developed four more nodules in the skin Her general condition was rapidly deteriorating and she complained of headache and pain in the right shoulder region Skiagrams of the affected parts did not show any evidence of secondary deposits She developed oedema of the right hand which spread

upto the forearm, the arm and the right side of the chest and ultimately involved the face. She expired on the 22nd day after admission. An autopsy could not be obtained.

This case came with signs highly suggestive of malignancy. The interesting point was the determination of the site of primary in view of a nodule in the thyroid gland. The diagnosis was established by a biopsy of the secondary skin deposit, where the typical thyroid structure was not seen and the primary was considered to be in the lung.

*Case 2*—J. D., a Deccani Hindu female of 55 years, was admitted for dyspnoea, cough, pain in the right side of the chest and swelling of the face and the arms.

Her complaints started about seven months before admission when she developed pain in the right side of the chest, oedema of the right upper extremity and the face. She had been dyspnoeic for four months prior to her admission and her complaints were gradually increasing from day to day. There was no fever or haemoptysis at any time during the course of these seven months. No family history of tuberculosis could be obtained.

On examination she was seen to have oedema of the right upper extremity, the right thoracic wall and the face, which was pitting on pressure. The right breast was distended and oedematous. There were dilated and tortuous veins on the right half of the chest wall and the blood was flowing in them from above downwards. The lymph nodes in the neck or axilla were not palpable. There was a subcutaneous nodule 2"  $\times$  3" in the right infra-mammary area which was hard to feel. The nails showed early evidence of clubbing which was more easily noticed on the right side. There were signs of effusion in the right pleural cavity upto the level of the 4th rib in the axilla, with signs of consolidation above this level. There was marked engorgement of the right external jugular vein. The apex beat was in the fifth intercostal space 5 inches to the left of the mid-sternal line. The heart sounds were normal and regular, B.P. 100/60 on both sides. Liver and spleen were not palpable and there were no other abnormal findings.

R.B.C. 43 million per c.mm (on admission), 25 million per c.mm (8 weeks later), Hb 75 per cent, and 40 per cent, W.B.C. 8900 per c.mm, P 68 per cent, E nil, B nil, L 28 per cent, L.M. 4 per cent, Kahn test, negative.

Sputum.—No elastic fibres, tubercle bacilli or malignant cells seen. Urine and Stool N.A.D.

Screening of chest.—Dense opacity on the right side upto the level of the 3rd rib anteriorly, the upper margin of which was not sharply defined. The right phrenico-costal sinus was obliterated. The upper lobe of the right lung was seen to be hazy as compared to the left side. Movements of the right cupola of the diaphragm were not seen. The mediastinum was pushed to the left by about 1½ inch. The left lung field was normal.

Skiagram of the chest after paracentesis thoracis showed an opacity in the right lung field starting from the hilum and going towards the periphery in a fan-shaped manner. The ribs and the thoracic vertebrae were normal.

Skiagram of skull and both upper arms showed no evidence of secondary deposits.

Pleural fluid was light brown in colour with traces of fibrin and blood, with 48 cells per cmm mostly lymphocytes, and showed large clumps of deeply staining cells showing variation in their sizes. Sections of the subcutaneous nodule showed merely a calcified mass in a fibrous capsule.

While under observation the patient developed marked clubbing of the fingers in about eight weeks time. The oedema of the face and the right upper extremity became considerably less, after she had developed a marked collateral circulation on the anterior aspect of the chest and the abdomen. The patient's breathlessness, however, went on gradually increasing until she died about 2½ months after admission.

An autopsy was performed and the upper and middle lobes of the right lung were seen to be infiltrated with a dense hilus type of growth. The right lower lobe was collapsed. There were secondary deposits in the left lung, the pericardium, the heart wall and the liver. The hilar glands were enlarged. The right innominate vein was pressed upon and showed a thrombus which however was not invading the superior vena cava. The mucosa at the bifurcation of the right bronchus was roughened, suggesting the primary site of the growth.

The noteworthy feature of this case was the unilateral oedema, due to obstruction to the venous flow, which was markedly relieved when the collateral circulation was established. Dormer, Friedlander and Wiles have described a similar case where the growth itself had infiltrated the left auricle and invaded the left pulmonary vein.

\*Case 3—KPS, a Cutchi Bania male, aged 22, grain dealer was admitted in the hospital in a moribund condition.

A year and half ago, the patient had been operated for a small swelling, near the outer angle of the right eye, which was painless to start with, about the size of an almond and of 4 years' duration. This was excised *en masse* and the wound healed completely. About six months later there was a recurrence of the swelling in the old scar, with enlargement of the glands at the angle of the jaw. The swelling was painful, very hard and fixed to the glands underneath. The swelling and the glands were excised, taking them to be fibrosarcomatous, but a section report revealed an extremely de-differentiated carcinoma.

A month or so after removal of this growth the patient began to feel extremely tired, breathless and forced to take to bed. Within a few days he had recurrence of the swelling and developed a lump in

the epigastric region. The vision of his right eye became hazy and his friends noticed that his right eye-ball had protruded from its socket. The original swelling became multilobular and several other subcutaneous swellings appeared in the neck, chest wall, right thigh and the gluteal region. A few days before admission he developed jaundice which went on becoming deeper and deeper every day. He had occasional vomiting.

When seen in the hospital the patient was in a moribund state the whole body was of a dark greenish yellow colour and markedly emaciated. There was a well marked proptosis of the right eye with



Fig. 2—Case 3 (Dr N D Patel's case)

marked chemosis of the conjunctiva. There were multiple nodular swellings on the body. The swelling in the right fronto-parieto-temporal region was multilobular, four by six inches in size, hard in consistency with a few areas of softening towards the centre. The skin over it was red, tense, warm and shining. The swelling was fixed to the bone and its edges could not be demarcated. There was a hard multilobular lump in the epigastrium  $3'' \times 2''$  intra-abdominal and not moving with respiration, which seemed to be continuous with the liver. The liver dullness extended three fingers breadth beyond the right costal margin and was in continuity with the epigastric

lump The spleen was not palpable, there was no ascites Except for hurried respirations and signs of basal congestion, nothing abnormal was found in the respiratory system

The heart margins could not be made out, the apex beat was neither visible nor palpable and the heart sounds were distant and feeble There were no foreign sounds The rhythm was irregular due to presence of multiple extra-systoles BP was 110/60 mm of mercury R B C 23 mill per cu mm Hb 38 per cent, C I 0.8 W B C 21,000/ per cu mm P 71 per cent, L 29 per cent, M E & B nil Urine showed excess of bile pigment

The orbital tumour with enlargement of liver and evidence of secondaries in the heart, skin and lymph nodes suggested the diagnosis of a lymphosarcoma or a malignant melanoma The involvement of the right orbit with enlargement of the liver was very suggestive of Hutchinson's neuroblastoma of the right adrenal but the age of the patient was against the diagnosis

The patient expired two days after admission and the post-mortem examination showed enlargement of lymph nodes in the abdomen with adhesions to the stomach, pancreas and intestine This mass of enlarged glands caused obstruction of the biliary ducts There were no metastasis in the liver, the right suprarenal was normal but the left was enlarged and replaced by a growth There were malignant deposits in the lungs, wall of the heart, skull, dura mater and the right orbital cavity There were no metastasis in the brain For some time there was a doubt about the nature of the malignant process in the case, but after a very careful consideration of the sections a diagnosis of bronchogenic carcinoma was arrived at

*Case 4*—P.N, a Hindu male aged 50, pressman by occupation, was admitted in the K. E M Hospital for continuous cough with expectoration and pain in the right side of the chest in the axillary region, of seven months' duration The pain was sudden in onset and was exaggerated by deep breathing and coughing A week after the onset of pain the patient developed a continuous and troublesome cough with very scanty expectoration The pain as well as the cough though never completely relieved lessened in intensity after about 3 months during which he was treated by local medical practitioners and he felt much better at the time of admission But the trouble which brought him to the hospital was a loss of 36 lbs in weight during the seven months of illness and he was afraid he had developed pulmonary tuberculosis There was no history of fever or blood stained sputum or haemoptysis at any time during this illness There was no history of pulmonary tuberculosis in the family His temperature was 98°F, pulse 100 per minute and respirations 20 per minute The only positive physical finding was a slight impairment of percussion note at the right base with markedly deficient breath sounds and voice sounds without any foreign sounds There was no evidence of shifting of the mediastinum His sputum did not show any T.B. by routine and concentration methods R B C count was 51 million per c.mm Hb 84 per cent, C.I-0.8 W B C 10,500

per cum mm P 77, E 4, L 16, LM 30 per cent Stools did not show any evidence of amoebic colitis Fluoroscopic examination showed a localised opacity at the right base in the perihilar region The right phrenico-costal sinus was clear, the movements of the diaphragm on the right side were normal and there was no shifting of the mediastinum A diagnosis of collapse of the right middle lobe was made and a bronchoscopic examination was carried out This revealed marked oedema and congestion of the mucous membrane lining the right middle bronchus which was entirely obliterating the lumen There was also oedema of the left lower bronchus but the lumen was patent though narrower than that of the left upper bronchus A section was taken from the right middle bronchus and a bronchography was done The right upper bronchus and both the bronchi on the left side allowed the iodised poppyseed oil to pass through, but the right middle and lower bronchi were completely obstructed A probable diagnosis of bronchogenic carcinoma was made and the patient was discharged and referred to the Tata Memorial Hospital A fortnight later he was again admitted in the K.E.M Hospital for severe pain all over the body This time the clinical examination showed over and above the previous findings, an enlarged tender liver and hemiplegia on the left side These evidences of metastasis in the liver and the brain confirmed the diagnosis of bronchogenic carcinoma The patient went away against medical advice the same evening

Case 5.—P F, a Christian male aged about 50, was admitted in the K E M Hospital in a moribund condition with oedema of both feet both lungs full of moist sounds, and a mass of hard glands in the right side of the neck This patient had attended O.P.D of the hospital about six months before this for cough and haemoptysis Impairment of note and coarse rales were detected at that time on the right apex and on screening of the lungs infiltration in the right apex was reported The patient was straightaway given a memo and was advised to attend a tuberculosis dispensary but his sputum was not examined The patient died within an hour and a half of admission and an autopsy was performed This showed a squamous carcinoma of the right eparterial bronchus with infiltration at the right apex and metastasis in the right lung, the mediastinal lymph nodes, cervical lymph nodes on the right side and the suprarenals on both sides Besides these, the right lung showed bronchiectasis, broncho-pneumonia and abscess formation in the lower lobe Another interesting point about this case was the congenital absence of penis with urethral opening posterior to the scrotum

Case 6.—J F, a Christian male sea-man aged 45, was admitted in the K.E.M Hospital for increasing dyspnoea and cough with expectoration for 3 months The complaints started gradually and went on increasing till the patient became orthopnoeic and was somewhat relieved on sitting up and leaning forward on a cardiac table There was no history of haemoptysis and no history of fever He gave history of exposure followed by a sore on the penis 15 years ago

On examination there was marked respiratory distress, the alae nasi were moving, there was clubbing of fingers and the cervical and inguinal lymph nodes were enlarged, hard and discrete. There was an area of dullness on the left of the sternum in the 2nd and 3rd intercostal spaces, continuous with the upper border of cardiac dullness. The left border of the heart was  $3/4$  inch beyond the mid-clavicular line in the left 5th intercostal space. There were crepitations at both the lung bases, liver and spleen were not palpable and CNS was normal. The pupils were equal on both sides but the pulse was feeble on the left side. The BP was 140/100 mm of Hg on the right side and 120/70 mm of Hg on the left side. The venous pressure was 12.8 cms of water on the right side and 20.5 cm of water on the left side. His WBC count was 9000 per c.mm with P 59 per cent, E 3 per cent,



Fig 3 —Case 6 (Dr N D Patel's case)

and L 38 per cent, and the Kahn flocculation test was negative. The sputum was repeatedly negative for mycobacterium tuberculosis. On screening there was an opacity in the superior and posterior mediastinum continuous with the aortic shadow with doubtful pulsations and there was enlargement of the left ventricle. In view of these findings a diagnosis of syphilitic aneurysm of the descending part of the arch of the aorta was given. Three days after admission, however, the patient complained of severe pain along the left side of the neck and inability to turn his neck from side to side and two days later an examination of his nervous system showed exaggerated tendon reflexes in the lower limb with a doubtful extensor plantar response on the right side and flexor response on the left side. The sensation of pain and touch was diminished below the level of the

umbilicus The deep sensations were normal Two days later there was definite exaggeration of all the deep reflexes in the lower limbs with bilateral ankle clonus and bilateral Babinski response with loss of cremasteric and abdominal reflexes This sudden change in the clinical picture gave rise to suspicion of malignancy of the lung with erosion of the vertebrae From that day the patient rapidly deteriorated in health, developed a spreading bed sore on the sacrum, had retention of urine and irregular temperature and became incoherent in thought and speech He expired five days after this An autopsy revealed a fusiform dilatation of the ascending part of the aorta with syphilitic and atheromatous changes The mediastinal and bronchial lymph nodes were enlarged, hard and adherent The left bronchus showed a growth with collapse, broncho-pneumonia and abscess formation in the lower lobe There were metastasis in the right 3rd and left 5th ribs and the dorsal 4th and 5th vertebrae with pathological fractures

Case 7—S G, a Hindu male aged 50, supervisor of coolies doing loading and unloading work in docks and railways, was admitted in the KEM Hospital for haemoptysis on and off for 1 month The complaint started with slight irregular temperature for about a week associated with blood stained sputum This was followed by coughing out of cup-full of blood on two occasions, and the patient again started running an irregular temperature with a maximum of 100°F There was no breathlessness but the patient was feeling extremely weak There was no history of tuberculosis in the family

On examination the patient was found to be well built with pallor of nails and conjunctivae and oedema of both feet pitting on pressure There was diminished movement on the right side of the chest, impairment of note all over the right side below the first interspace, diminished air entry and a few crepitations at the right base There was no displacement of the mediastinum Nothing abnormal was detected in the cardiovascular system The liver was enlarged and had a nodular feel P R the prostate was felt to be enlarged with obliteration of lateral sulci The rectal mucosa was not freely moveable over the prostate His R.B.C count was 4.06 mil per cmm Hb 70 per cent, W.B.C 10350 per cmm, P 73 per cent, B 2 per cent, L 25 per cent, Kahn test was negative The sputum was repeatedly negative for mycobacterium tuberculosis and no malignant cells were seen when examined by the ordinary method Screening of the chest showed a dense opacity on the right side upto the 2nd rib There was no displacement of the trachea or the mediastinum A sternal smear did not reveal the presence of any malignant cells On bronchoscopic examination we found narrowing of the right middle bronchus with oedematous mucosa which bled rapidly on touch No definite polypoid or protruding growth was seen A section, however, was taken from this mucosa and was reported to be a bronchogenic carcinoma Two days after bronchoscopy the patient had severe respiratory distress, became cold and clammy all of a sud-



den and expired within half an hour Unfortunately no autopsy could be obtained

Case 8—G N, a retired Hindu male aged 75, was admitted in the KEM Hospital for unconsciousness of 3 days' duration The doctor who had referred the case to the Hospital said that the patient was a subject of diabetes and had not passed urine for 3 days and stool for 5 days The patient was in a moribund condition with deep stertorous respiration and cyanosis The heart sounds were feeble and pulse was thready There was a lump about 4 cm in diameter on the posterior aspect of the right shoulder fixed to the deeper structures and ulcerated at the summit There was a bullous of eruption in the right hypochondrium from a probable burn Both the lungs were full of moist sounds With the history of diabetes and coma a probable diagnosis of diabetic coma was made but the urine did not show any evidence of sugar or ketone bodies The patient expired within ½ hour of admission An autopsy was performed and the findings were as follows—Enlarged, hard lymph nodes in the submandibular region right side, no enlargement of lymph nodes in the axillary or cervical region The right lung showed a perihilar hard growth in the middle lobe The tracheo-bronchial lymph nodes on the right side were enlarged and hard The left lung was bulky and oedematous There was a whitish nodule of secondary deposit about 0.75 cm in diameter in the wall of the left ventricle There was also a hard nodule in the right side of anterior 2/3 of tongue 3 cm × 5 cm which on section showed a diffuse infiltration with malignant cells The pancreas was hard to feel at places and there were two hard nodules on section about 2 cm in diameter There was no obstruction to the bile duct The section showed infiltration with malignant cells There were secondary deposits in the adrenals and the wall of the gall bladder In the right occipital lobe of the brain there was metastasis undergoing liquefaction which on microscopic section showed necrosis, haemorrhage and a peritheliomatous arrangement of malignant cells The skin nodule showed metastasis in the dermis and the subcutaneous tissue with hydropic degeneration in the stratum spinosum The microscopic section of the lung showed large polyhedral malignant cells with pseudo-adenomatous arrangement at places and diffuse at others Normal structure of the lung was completely lost There was an infiltration of bronchiolar wall with same type of cells suggesting alveolar carcinoma

*(To be continued next month)*

# Critical Notes & Abstracts

## THIOURACIL AND THIOUREA IN THE TREATMENT OF THYROTOXICOSIS

(H P Himsworth, M D, F R C P, *Clinical Journal*, LVIV, pp 97-104, 1945)

In 1943 E B Astwood reported the beneficial effects of treating cases of thyrotoxicosis with either thiourea or thiouracil. His claims, as far as they concerned the initial effects of these drugs, were soon confirmed on small groups of cases by Williams and Bissell (1943) and by Himsworth (1943). The purpose of this communication is to report the results of more extended experience.

When the treatment was first used in England only thiourea was available, but later thiouracil was obtained. The action of both these drugs on thyrotoxicosis is similar, but thiouracil has distinct advantages over thiourea in not producing the unpleasant smell in the breath, the conjunctivitis or the vomiting which frequently attend the use of the latter preparation. These advantages quickly led to the exclusive use of thiouracil, and in this paper, unless otherwise stated, the results have been obtained with that drug.

During the last ten months 33 cases of thyrotoxicosis have been treated by one or other, or both, of these drugs at University College Hospital, 26 of them were under my direct care, and 22 of these have been observed beyond the period of initial treatment. The longest period of observation is ten months, the shortest ten weeks. Of these 22 cases, 7 were treated initially with thiourea and subsequently with thiouracil, the remaining 15 with thiouracil throughout. For convenience of discussion the results will be considered under the headings of initial treatment, maintenance treatment, symptoms of over-dosage and idiosyncrasy to the drugs.

### INITIAL TREATMENT

The period of initial treatment lasted until a conspicuous regression of the subjective and objective signs of thyrotoxicosis showed that the illness was largely under control. Its average duration was 29 days. The dose of thiourea used during this period was 1 g three times a day, the dose of thiouracil 0.2 g five times a day. In no case, irrespective of its type, severity, or duration, did the treatment fail to produce conspicuous improvement, and none became drug-resistant. The objective evidence of this is summarized in the table.

TABLE

<i>Thiourea and Thiouracil Treatment</i>	<i>Initial Course of Treatment</i>	<i>Results in Group 1 (22 Patients)</i>
Dosage	Thiourea 3 g daily or thiouracil 1 g daily	
Duration of initial course	Average 29.3 days	
Weight change	All gained. Average 7.7 lb (range 2 to 15 lb)	
B.M.R.	1 fell in all. Before (average) + 39.7 (range + 18 to + 82) After (average) + 8.6 (range + 20 to - 14)	
Pulse rate	Fell in all. Before (average) 100 day, 87 night. After (average) 80 day, 74 night	
Plasma cholesterol	Rose in all. Before (average) 127 mg/100 ml (range 83 to 166) After (average) 186 mg/100 ml (range 125 to 310)	

It will be seen that in every case the pulse-rate and basal metabolic rate fell, while the plasma cholesterol and body-weight rose (Table). The improvement in symptoms was similarly marked. The sweating, skin flush and nervousness disappeared and diarrhoea, if present, stopped. Two of the cases were fibrillating before treatment was given. One, whose fibrillation was intermittent, became consistently regular, the second, after the pulse-rate had been reduced by thiouracil, was brought back to normal rhythm with quinidine and remained normal. The effect on the eye signs and goitre was less marked. Lid retraction always decreased, but exophthalmos was not noticeably altered. In the majority of cases the goitre was unaffected and, in those in which it did decrease, the decrease appeared attributable to diminished vascularity rather than to reduction of glandular tissue. It seems, therefore, that thiouracil and thiourea influence only those symptoms of thyrotoxicosis referable to over-function of the thyroid gland, affecting slightly, if at all, those symptoms, such as the goitre itself and exophthalmos, which are believed to arise from causes outside the gland.

Thiouracil acts neither immediately nor uniformly upon the symptoms and signs of thyrotoxicosis. The delay before its action varies in different patients. Usually little change is seen in the first and second weeks of treatment, but by the third it is evident, and by the fourth established. In some patients however a good response occurs within a few days, in others the response is slow and takes six, eight or more weeks to become established. This latter delayed reaction occurs particularly in patients who, immediately before, have been treated with iodine, and in such cases it is advisable to withhold iodine for one or two months before beginning treatment with thiouracil.

When the treatment begins to take effect the individual symptoms are not all affected proportionately and at the same time. Usually the skin flush disappears early and the raised pulse-rate persists longest. Sweating, nervousness, raised metabolic rate, emaciation and low plasma cholesterol begin to yield at intermediate times, and generally speaking, in that order. Failure to recognize this sequence in effects has led to certain slow-reacting cases being classified as thiouracil-resistant. Three such cases have been referred to me. In each the subjective improvement, falling basal metabolic rate, and rising weight curve showed that the thyrotoxicosis was being brought under control. The contrary impression was derived from the continued elevation of the pulse-rate, and with further treatment, this returned slowly to normal levels.

There thus appears to be no question that by means of thiouracil, or thiourea, thyrotoxicosis can rapidly and effectively be brought under control, and that the results of the initial treatment with these drugs are comparable to those achieved by surgery.

It was early realized (Astwood, 1943) that, after the initial course, thiouracil treatment must be maintained at least for some time. But it became evident that far smaller doses were required for

maintenance treatment than to establish control, and that it was important to allow for this if symptoms of overdosage were to be avoided. This decrease in requirements is most striking in the early stages but it extends beyond a simple initial readjustment of dosage and there are indications that it may be progressive.

We have been reducing the maintenance dosage more and more rapidly. Most of our patients are now taking 0.1 g. or 0.05 g. daily, and in no case has a return of symptoms or a fall in weight suggested that the reduction has been too rapid or too much. This consideration is of particular importance in view of the dangers due to overdosage with the drug.

It would appear that a mechanism exists in the body which resists attempts to force the metabolism below normal. If this were not so then treatment should always produce a steady decrease of metabolism. This does not usually occur in man. As a basal metabolic rate approaches normal its fall slows, even though the dose of thiouracil remains unchanged. Having reached normal, there it tends to remain, and its persistence at this level despite subsequent lightening of dosage suggests that further depression of metabolism is being resisted. The practical importance of this consideration is that evidence of subnormal metabolism should not be awaited before reducing the dose of thiouracil. The dose should be decreased rapidly and continuously until there is evidence that it is insufficient. Then the dose is adjusted appropriately and retained at that level for a few weeks, when a further attempt at reduction is made.

The success of any therapeutic method must ultimately be judged by the efficiency with which it restores the patient to normal. In this respect, for periods up to ten months, thiouracil compares favourably with other methods of treating thyrotoxicosis. The majority of patients feel fit to resume full work in one to three months after completion of the initial treatment and, having started, are able to continue. The severity and responsibility of the work offer no bar. One patient is doing full duty as a London bus driver, another occupying a responsible managerial position, many are looking after their families unaided, and several have returned to industrial work. The disabling symptoms of Graves's disease are thus effectively controlled. But there are two signs which do not appear to be altered significantly even by prolonged treatment, these are exophthalmos and goitre. In two cases, not in my own series, the goitre had eventually to be removed because of pressure symptoms.

It is as yet too early to form an opinion whether treatment with thiouracil can ultimately be discontinued and the patient remain well. Undoubtedly omission of treatment in the early stages is followed by a return of symptoms, but there are hints that later such may not be the result. One of my patients after treatment with thiourea for 70 days discontinued the drug and has had no treatment for 5 months. There has been no return of symptoms and she has maintained her weight. Two others have been off treatment with thiouracil for 5 and 7 weeks respectively without showing any untoward

effects. None of these cases was severe, and before omission of treatment all had been weaned on to very small doses of the drug. It remains to be seen whether their present freedom from thyrotoxic symptoms will be maintained, and whether or not this favourable result is unusual\*.

#### OVERDOSAGE

If thiouracil and thiourea had no untoward effects, it would now be reasonably certain that an efficient medical treatment of thyrotoxicosis had been devised. Unfortunately they have such effects, and only experience can show whether these occur so frequently as to render treatment with these drugs more dangerous than surgical removal of the gland. In considering their ill-effects it is important to distinguish the effects due to overdosage from those due to idiosyncrasy. By the manifestations of overdosage are meant those symptoms which can be induced in any patient by excessive doses of the drug. By the manifestations of idiosyncrasy are meant those conditions which occur capriciously and inconstantly in a minority of patients.

The manifestations of overdosage can be divided into two groups. The first, which is easily recognised and avoided, occurs early in treatment and from gross overdosage. The second develops insidiously and then quickly becomes manifest, and apparently results from chronic, slight overdosage. *Gross overdosage* shows itself by an increase in size, sometimes painful, of the goitre. Our first case was discharged from hospital on 2 g of thiourea daily. He then wore a 15½ in collar. Within the next two months his goitre increased in size so that a 17 in collar was too small. On reducing the dose to 0.5 g daily the goitre slowly decreased to its original size. A second mild case who had previously undergone a subtotal thyroidectomy, developed painful nodules all along the operation scar. A third case with a retrosternal goitre developed pressure symptoms. Since adopting a more rapid reduction of dosage after the initial course of treatment few cases of this kind have been seen, and on further reduction of the dose these have all been rapidly relieved.

*Chronic, slight overdosage* shows itself mainly by subjective symptoms. A patient who for weeks or months has been on the same small dose of thiouracil, and who has previously continued to remark on her improved well-being, comes up complaining of weariness and depression. Not infrequently such cases have a bloated appearance and their friends remark on their lack of energy. Superficially the evidence suggests hypothyroidism, but inspection of the weight chart usually shows that the weight has been constant for weeks, and determination of the basal metabolic rate shows no depression. This state is associated with, and often preceded by, an elevation of the plasma cholesterol. On reducing the dose the symptoms rapidly disappear and the plasma cholesterol falls. In passing it should be noted that

\* Since the above was written in June 1944 4 patients who have been off treatment from 7 to 12 months and 3 who have been off treatment from 3 to 6 months have been observed. The average duration of treatment in these was 9 months and before its omission all had been weaned on to small doses of thiouracil for long periods. None has relapsed. A further patient after 8 months treatment omitted the drug for four months and then had a mild relapse during severe air raids.

these symptoms are not associated with alteration in the white blood-cell count. There is insufficient evidence available at present to decide on the pathogenesis of these symptoms. Are they indeed the first signs of rapidly developing hypothyroidism, or are they the results of a toxic action of the drug? The former explanation appears the more probable. But whatever the explanation, this type of overdosage is particularly prone to develop during maintenance treatment, and can be avoided by reducing the dose to the minimum required to maintain the weight. As a further check the blood cholesterol level can be determined periodically and, if this is rising unduly, the dose of thiouracil should be reduced.

#### IDIOSYNCRASY

*Fever, rashes, enlargement of lymph glands and blood changes* have been reported as manifestations of sensitivity to thiouracil (Astwood, 1943, Gabilove and Kert, 1944, Newcombe and Deane, 1944). *Fever* occurred in 3 of the 33 cases. In 2 it could be accounted for by a coincident infection, one patient having a streptococcal infection of the throat, the other an active infection by *B. coli* of the urinary tract. In both cases the temperature subsided with the infection, and did not rise when thiouracil was again given. In the third case no infective cause was found. The fever occurred after the patient had been taking 1g of thiouracil daily for eight days and as, unlike the other two, it was associated with a neutropenia, the drug was discontinued. The temperature then fell. One patient showed a *maculopapular rash* on the fifteenth day of therapy with 1 g of thiouracil daily. As it was unassociated with either fever or leucopenia the drug was continued, though at the reduced dose of 0.4 g daily, and the rash faded during the next three days. *Enlargement of lymph glands* has not been observed in our series.

These three manifestations of sensitivity resemble those occurring after many other drugs, not only in their nature, but in the delay before their appearance. All have been reported as occurring within a fortnight or so of exposure to the drug, and they have not been observed after this time, even in cases which have been under treatment for many months. Their appearance early in treatment may be due to the heavy doses of the drug used in the first fortnight, but that this is not the most important factor in their production is evident from the fact that the majority of patients take such doses with impunity. A special sensitivity to the drug is presumably present in the persons affected. In that case the failure of these particular ill-effects to appear after the first fortnight suggests either that the sensitive subjects are few in number and eliminated by early detection, or that desensitization is effected by continued treatment.

The most serious manifestations of sensitivity are those which affect the formed elements of the blood. *Leucopenia, agranulocytosis* (Astwood, 1943) and *thrombocytopenia* (Newcombe and Deane, 1944) have been reported. The latter has not occurred in our series, but there have been two cases of leucopenia and one case of agranulocytosis out of the 33 cases. The first case of leucopenia was the above

patient with the unexplained temperature. At the beginning of the febrile attack the white blood-cell count had fallen from 7800 with 84 per cent of neutrophils to 2000. At the height of the fever it was 4400 with 35 per cent neutrophils. The second case received 1 g of thiouracil daily for fourteen days, when a routine blood count showed 1100 white cells with 50 per cent neutrophils. Treatment was discontinued and the blood count rose. This patient had no untoward symptoms throughout. The third case had, on admission, a white count of 10,000 with 68 per cent neutrophils. After treatment for one month with 1 g of thiouracil daily no improvement in the thyrotoxicosis had occurred. This was attributed to her having received iodine daily for two years before admission. As there had been no toxic symptoms and the white cell count was 9300 the dose of thiouracil was raised to 2 g daily. At the end of a further fortnight the thyrotoxicosis had responded, the white cell count was 6000 with 60 per cent of neutrophils, and the patient was discharged on 0.6 g daily. Eight days after discharge she developed a whitlow, two days later she felt chilled, the temperature rose to 104° F, and two days after she developed a sore throat. On admission she had 1500 white cells with no neutrophils and only a few primitive cells were present in the sternal marrow. Vigorous treatment with fresh blood transfusions and pentnucleotide was given. Neutrophils returned to the blood four days later. Six days after admission the white count was 26,000 with 76 per cent of neutrophils and the sternal marrow showed vigorous activity and mature cells. Then, unfortunately, she contracted a bronchopneumonia and from this she died.

*Aggranulocytosis* being the most dangerous complication of treatment with thiouracil or thiourea, it is important to consider the factors concerned in its production. It is evident that idiosyncrasy plays a part. If an invariable action of these drugs were to depress the production of neutrophils, then it would be expected that these would fall in all patients. This does not happen. In the series of 22 patients shown in the table the white cell counts on admission ranged from 4000 to 10,000 with an average of 6513, the neutrophils ranged from 42 per cent to 80 per cent with an average of 59.3 per cent. On the completion of the initial treatment the white counts ranged from 3000 to 11,600 and averaged 6865, the neutrophils ranged from 40 per cent to 81 per cent and averaged 50.6 per cent. Throughout the period of maintenance treatment white cell counts have been done on all patients at intervals of not more than one month. Again there is no evidence of a consistent and steady depression of neutrophils as treatment continues. Neutropenia, when it occurs, appears suddenly in patients whose previous blood counts have been normal both in respect of total white cells and total neutrophils. There is a hint, however, that its supervention may be foreshadowed by the appearance of many young neutrophils in the peripheral blood. This possibility is being investigated. Lastly, neutropenia does not develop until a week or more after treatment has commenced—an observation which may be explained either by a cumulative toxic effect or a deve-

loping sensitivity Despite this evidence of idiosyncrasy, there is however, an indication that the development of neutropenia is also influenced by the dose of thiouracil used, not by the total dose given over many months but by the intensity of the daily dosage The three cases reported here all occurred either during or shortly after intensive treatment Astwood's fatal case was receiving 2 g of thiouracil daily, Newcombe and Deane's case of thrombocytopenia and leucopenia had taken 83 g of thiourea in five weeks, and a third fatal case, of which I have been informed, had received 103 g of thiourea and 62 g of thiouracil in five months As far as I am aware no cases have been reported of any manifestations of sensitivity in patients taking thiouracil in small doses of the order of 0.1 or 0.05 g a day

It thus appears that two factors are involved in the production of this untoward effect of thiouracil *idiosyncrasy and dosage* If this be so, then we may hope to avoid it by using small doses of the drug For this reason, and because of the evidence that the maintenance doses have been greater than necessary, it seems advisable to use, in all stages of the treatment, smaller doses of thiouracil than have been used up to now The dosage which is being used at present is 0.6 g daily until the B.M.R. falls to about +10 per cent Thereafter the dose is decreased to 0.1 g or 0.05 g daily during the maintenance period It is hoped, on the basis of analogy with the sulphonamide drugs, that by using these smaller doses and reducing the dose more rapidly a safe yet effective technique of this promising therapy may be evolved For the present, however, it should be realized that thiouracil therapy is still in the experimental stage, and that it should only be used under circumstances which allow close, detailed and continued investigation of the patients

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## Notes on New Drugs

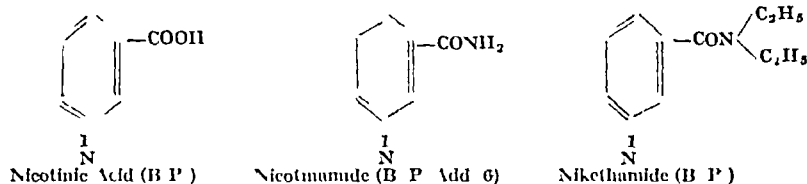
**NIKETHAMIDE**, by Thomas Draper, M.D., (Missionary Medical College, Vellore)

Nikethamidum B.P. (3rd addendum), is not a new preparation as it has been in use for at least fifteen years under the name of Coramine (Ciba) and more recently as Anacardone (B.D.H.) It has now obtained official status, and rightly so, inasmuch as it is one of the really valuable medicines to be found in the physician's armamentarium One of the first points of interest we notice is that of its close (chemical) relationship to an acid of the vitamin B complex,



now officially known Acidum nicotinicum BP (add 4) Nicotinic acid is Pyridine—2—carboxylic acid, a comparatively simple chemical substance

Nikethamide is Pyridine —3—Carboxy—diethyl amide,  $C_6H_4NCON(C_2H_5)_2$ , and as given below the structural relationship will be readily seen



It is not claimed for this drug that it has any *direct* action on the cardiovascular system, rather does it belong to the class of substances known as Analeptics (Cordial, Restorative) The action of Nikethamide on the heart, unlike that of Digitalis, is exerted through the central nervous system, probably through spinal reflexes, and stimulates the respiratory centre in the medulla, thus the depth and frequency of respiration are increased, the vaso-motor centre is stimulated, the peripheral blood vessels are constricted, the blood pressure is raised and the force of the cardiac contraction is increased According to some authorities the drug also improves the coronary circulation of the heart either by a vasodilating action on the coronary vessels or by an extrinsic nervous mechanism An indirect effect is that the restored respiration deepens the suction-pump action of the thorax, which is so important for the diastolic filling of the heart, whilst the general improvement in muscle tonus throughout the body accelerates the return of the venous blood to the heart When this drug was first introduced as Coramine the usual extravagant claims as to its all-embracing values were made, but today the drug has permanently established in the hands of clinicians both its limitations and its usefulness

Let me give you the conservative statement of United States Dispensatory (Ed 23) "Nikethamide was introduced as an analeptic in the stead of camphor The results of various investigators into its physiological action have been almost as contradictory as in the case of camphor Beiger (W M W, 1935 85 597) in a complete review of the literature studied up to that date concludes that it stimulates both the respiratory and vaso-motor centres in normal animals Stoland and Ginsberg (J.P exp T, 1937, 60, 396) believe that the variance of opinion by different experimenters is due to the fact that the action differs on different species of animals, in rabbits it causes a rise in blood pressure but in dogs a fall They find that it dilates the coronary artery in both animals Myers (J Hy 1940, 40, 474) confirms this action on the coronary artery and also finds that while it does not increase cardiac output of the normal heart it will excite the heart poisoned by chloral Nikethamide has been used as a respiratory stimulant especially against depressant poisons, it is apparently of value

in poisoning by morphine or chloral or tribromethyl alcohol (avertin) but comparatively inefficient in barbitol poisoning, Marshall (J P exp T 1937, 60, 472) It exerts a nicotinic acid effect and may be useful in pellagra but must be given in disproportionately large dose' (Smith, J P exp T 1940, 68, 458)

At this point I would like to state my own belief in reference to its inefficiency in the case of poisoning by the Barbiturates Recently three cases of poisoning have come to my notice The first was by Evipan Sodium where a large dose had been given to a woman over 70 previous to an operation for cataract This patient remained unconscious for four hours and two injections of coramine administered at one hour intervals had little effect upon her condition The second case was that of a woman (age 46) who took an unknown quantity of Soneryl tablets This patient died after an unconscious period of about 72 hours Coramine and all other measures failed to reconstitute her My third patient a female (age 32) took fifteen tablets of Dial as a single dose She was unconscious for 36 hours and then made an uneventful recovery Having previously been disappointed with the effects of coramine I did not in this case administer any, but relying on the more orthodox methods used in the treatment of poisoning by barbiturates succeeded in restoring consciousness There may be no harm in using Nikethamide for such cases but I suggest it is inadvisable to rely upon it to the exclusion of all other means should anyone be tempted so to do

Nikethamide B.P. is described as a colourless or yellowish oily liquid, or crystalline solid The dose is given in grammes and grains, 0.2 to 0.5 of the former, 3 to 8 of the latter By intravenous injection as a stimulant.—0.5 to 1.25 grammes, or 8 to 20 grains

Injection Nikethamide B.P. (4th add.) is a 25 per cent solution of the above Notice that the substance is stable enough to be sterilised in an autoclave The dose by subcutaneous or intramuscular injection is 1 to 4 mls., 15 to 60 minims, by intravenous injection as a convulsant,—5 to 16 mls., 75 to 240 minims

## THIOURACIL

*Indication*—For the treatment of thyrotoxicosis (a) primary, (b) toxic adenoma, and (c) thyrotoxicosis recurrent after partial thyroidectomy Presence of other endocrine disorders, pregnancy, or a low initial white cell count are not contraindications to treatment Cases of tachycardia and high B.M.R. that are not truly thyrogenic will not respond Cases modified by recent iodine therapy are refractory to thiouracil until their iodine stores are used up

*Mode of action*—Thiouracil acts by competing with the thyroid for iodine, the gland being starved of iodine cannot put out thyroxine, though it becomes cytologically more active while influence of thiouracil lasts The persistent activity of the anterior pituitary induces enlargement of the individual thyroid cells surrounding depleted alveolus

*Absorption and Distribution*—Quickly absorbed from gastro-intestinal tract to be distributed throughout the body tissues and fluids

About one-third of the ingested drug is excreted unchanged in the urine, none in the faeces

**Dosage.**—Initial dosage should never exceed 600 mg daily, in three to five divided doses To be stepped down as resting pulse-rate and B.M.R fall and symptoms abate The lower the daily total the less division is needed Recovered cases need maintenance of 50 to 100 mg, once daily

**Overdosage**—Shown by rapid significant enlargement of the thyroid, malaise, and apathy

**Idiosyncrasy**—In sensitised persons, fever, rash, adenitis, and blood cellular changes appear after a fortnight or so of taking the drug Serious manifestations such as marked leucopenia, agranulocytosis, and thrombocytopenia have been reported

**Clinical Effects**—Marked subjective improvement should precede all else, optimal recovery in two to eleven weeks, rapid drop in resting pulse-rate and the B.M.R after latent interval of two to twenty-six days B.M.R normal within a few weeks, with coincident rise of blood cholesterol While metabolic rate is still declining the patient regains weight and tremor, over-activity, sweating, peripheral vasodilatation, and vascularity of thyroid gland usually revert to normal

## Book Reviews and Notices

FOURTH ADDENDUM TO THE BRITISH PHARMACOPOEIA, 1932	Oct. 1941	p 59
FIFTH	"	" May 1942 p 42
SIXTH	"	" Aug. 1943 p 41

Price 5 s each Published for the General Medical Council by Constable & Co London.  
Bombay agents—Oxford University Press, Nicol Road, Bombay 1

We have received copies of the 4th, 5th and the 6th addenda to the B.P. of 1932, which became official in October 1941, May 1942 and August 1943 respectively In fact, these have been separately reviewed from the practitioners' point of view by Dr Merchant in this journal (*vide* Vol I p 401, 488, Vol III p 54,) and collectively by Dr Paranjpe in his series of articles on Recent Advances in Therapeutics with reference to the U.S.P. XII (*vide* Indian Physician, Vol II, pages 225, 263, 323) so that it is now too late and there is very little left to be said about them However, we may here bring out the following few points not referred to in those previous reviews The 4th addendum contains, besides new monographs and amendments to the "Old" ones, some appendices which are meant either as additions and amendments to these in the B.P. 1932 or its older addenda, but two of these are of some importance to the manufacturers, one on the determination of viscosity and the other describing special processes used in preparing solutions and suspensions for parenteral injection, including their sterilisation, both of them replace the corresponding portions in the B.P. 1932 and its addendum of 1936 The 5th addendum, in addition to new monographs and amendments, contains the cumulative index to the addenda I, II, III, IV and V The 6th addendum contains no special feature except the new additions, which have already been reviewed, and some amendments

# The Indian Physician

VOL IV NO 9

SEPTEMBER 1945

WHOLE NO 45

## Original Contributions

### BRONCHOGENIC CARCINOMA

A REVIEW OF THE LITERATURE WITH A REPORT OF  
EIGHT ILLUSTRATIVE CASES

by

M D MOTASHAW, M D (BOMB)

(Continued from page 180)

*Incidence*—Since the days of Nuschler who described a case of malignant disease of the lungs in a female child of 7 years in 1875 and of Betschart who described 4 cases of malignant disease of lung in 1895 many cases of carcinoma of the lung have been described to date. Since the beginning of the third decade of this century the role of carcinoma of the lung has changed from a subject of interest chiefly to the pathologist to a problem of major importance to the clinician. Jaffe of Vienna finds the incidence of carcinoma of the lung to be 10.73 per cent of all carcinoma in Vienna from 1915 to 1918 and the figure shows a slight rise to 11.47 per cent in 1935. In 1930 returns of the United States Cancer Institute, carcinoma of the lung constituted 28.95 per cent of all carcinomata in man and advanced from the fifth to the second place in the list of incidence of malignancy. It is not so commonly known that as many as 5,000 deaths occur annually from this disease in USA. (Adams et al, Surgery 11: 4: 503-42). Koletsky going over the 97 cases of carcinoma of the bronchus and lung that came to the autopsy room of the Cleveland City Hospital during the 11 years from 1927 to 1937 finds that its incidence is second only to malignancy of the stomach. Rosedale and McKay find that 75 per cent of all carcinomata are pulmonary in origin and stand third in the ranking list. Brines and Kenning find that 10 per cent of all carcinomata in 3000 serial autopsies in a general hospital in Germany are of pulmonary origin and they are second only to stomach malignancy in the ranking list.

This increase is not only present in the autopsy room returns but it is found that there is also an increase in the number of cases diagnosed ante-mortem. According to Lockwood only 5 per cent of cases of pulmonary malignancy were diagnosed ante-mortem in 1920 whereas as many as 50 per cent of them were diagnosed ante-mortem in 1938. But the question arises whether these figures not only suggest but also prove that there has been an actual increase in the

incidence of bronchogenic carcinoma. The apparent increase in the incidence may be due to a better understanding of the histopathology of bronchogenic carcinoma and its clear cut differentiation from the so-called mediastinal sarcomata in the autopsy room and also perhaps to the increased number of autopsies available in the recent times. The increase in the frequency of clinical diagnosis may be explained by the threefold facts that more people today live upto the cancer age than they did a hundred years ago, more people have become "cancer conscious" and seek medical advice instead of trying charlatan remedies, and that the increased facilities for diagnosis afforded to the cancer conscious medical man enables him to spot out more and more cases correctly. Menn and Anderson compared the relative incidence of the number of autopsies performed and the number of cases of bronchogenic carcinoma and plotted their curves for a period of 20 years from 1920 to 1940. They found that the two curves did not show a corresponding rise and fall but at times the curves were quite opposite to one another. This could be explained by the fact that the presence of an epidemic would decimate the population and cause an increase in the number of autopsies without increasing the number of cases of bronchogenic carcinoma.

Table I summarising the clinical and pathological findings in 8 cases of Bronchogenic Carcinoma (This is omitted to economise space—Editor)

The percentage incidence as found by various authors is shown in Table 2

Table 2 showing Incidence

Author	Percentage of total carcinoma	Sources of information	Year
Jaffe	10.73	Vienna	1913-1918
U S Cancer Institute	28.05	Hospitals of United states	1930
Jaffe	11.47	Vienna	1935
Koletsky	9.40	Cleveland City Hospital autopsy	1927-37
Rosedal & Mekey	7.05		1936
Brines & Kenning	10.00	3000 autopsies in Germany	1937

To the clinician it is not of very great importance to determine whether the increase in the incidence of bronchogenic carcinoma is apparent or real. Suffice it for him to know that he is likely to see more cases of bronchogenic carcinoma than his counterpart in the last generation, only if he would look out for them. During the years 1943 and 1944 there have been eight cases of definitely proved bronchogenic carcinoma under the care of my chiefs.

Like the aetiology of any other malignant disease we do not know what is the definite cause of bronchogenic carcinoma but any factor causing severe, prolonged or repeated respiratory infection or irritation producing repeated denuding and subsequent re-epithelialization of bronchial mucosa is likely to end in the establishment of a malignant pattern. Such factors held responsible are repeated attacks of influenza and pneumonia, pulmonary tuberculosis, industrial irritants like silica, coal dust, chromate dust, arsenical dust, asbestos dust and the oft quoted cobalt dust of Schneeberg cancer, irritation by

coal tar inhalation and inhalation of automobile exhaust, and exposure to radioactive substances. Even external trauma has been held responsible for the production of bronchogenic carcinoma but how far this is true, still remains to be proved. All the aforesaid irritants have been successfully employed by various workers including J. Argyll Campbell for producing bronchogenic carcinoma in mice but Singer believes that "Experimental production of bronchogenic carcinoma by the exposure of mice to coal tar fumes and to auto exhausts and by painting with tar and such carcinogenic substances has no co-relation to carcinoma in man because besides other considerations, cancer of the lung may occur spontaneously in mice (160 times in 6000 autopsies by Maude Slye). The irritating factor in automobile exhaust is phenanthrene and Cramer has shown that phenanthrene collected over the nasal, buccal, pharyngeal, laryngeal, tracheal and bronchial mucosa after an eight hour drive behind an automobile is only 15 mgm whereas that collected after smoking a 5 gm cigar is 200 mgms. Thus he believes that cigar smoking is a more potent cause of bronchogenic carcinoma than the increased use of automobiles. The increased frequency of bronchogenic carcinoma is taken as one of the curses of modern civilisation.

**Age**—The maximum incidence of bronchogenic carcinoma is found in the "cancer age" between 40 and 60 years, but the disease is fairly often seen beyond these limits also. The youngest case that could be found recorded in literature is by Schwytzer of a 16 months old child who died of diphtheria and on autopsy a bronchogenic carcinoma was found, (Quoted by Singer). Nuschler in 1875 described the case of a female child 7 years old who died of bronchogenic carcinoma. Simons in 1937 could find 4 recorded cases of primary carcinoma of lung below the age of 9 years and 6 more between the ages of 10 and 19. Brindley, working at the Mayo Clinic found one case below the age of 19 years in a series of 90 cases studied by him in 1944. 85.5 per cent of his cases were between 40 and 59 years of age, while Koletsky described 62 cases out of a series of 97 cases and Singer 209 (57.9 per cent out of a series of 361 cases in the same age group. Bela Halpert reviewing a series of 92 cases found 71 (77 per cent) cases above the age of 50 years. The details of the age-groups are summarised in Table 3.

Table 3 Age Incidence

Authors	Simons	Brindley	Koletsky	Singer	Bela Halpert
Total No. of cases	10	90	97	361	92
below 9	4	1		1 (Schwyter's quoted)	
between 10-19	0			13	
20-29		4			1
30-39		10	0	42	4
40-49		28	30	87	16
50-59		40	32	122	39
60-69		7	19	74	27
70-79			6	21	5
80-89			1	2	

*Sex*—The incidence of bronchogenic carcinoma is said to be higher in males than in females because the females are less exposed to the various irritants mentioned above and also because, carcinomata being mutually exclusive, the higher incidence of malignancy of generative organs reduces the susceptibility of the lungs in the female. But it has been remarked that the incidence in females is increasing because of spread of the fashions of civilization like smoking and greater employment of females in industry. The usual proportion given is 3 to 1 (Boyd) but Singer quotes a combination of various authors and finds that the proportion of males to females is as 405 to 131. But these authors do not give the relative percentage of the total male and female cases investigated and so these figures lose much of their authenticity and value. Bela Halpert, who investigated 4801 male necropsies and 2632 females, gives a proportion of 2.1. The figures given by other authors are shown in Table 4.

Table 4 Sex.

Author	Brindley	Halpert	Koletsky	Tinney	Singer	Combined
Male	70	80	87	370 (82%)	405 (81%)	1021 (81%)
Female	15	6	10	78 (18%)	131 (19%)	242 (19%)
Total	90	92	97	448	536	1263

*Pathology*—It is now agreed by all pathologists that "carcinoma of the lung arises primarily from the bronchial mucosa. The basal cells serve as the sole matrix for primary bronchogenic carcinoma and the other epithelial growths of the lung. These do not arise from metaplasia of pre-existing epithellum but through protoplasia of basal cells of the bronchial mucosa" (Fried quoted by Singer). Barnard in 1926 showed the presence of small oval cells with large polygonal cells, and tubules lined by columnar and cuboidal cells in tumours which were mostly composed of oat cells and were till then diagnosed as "oat cell sarcomata of the posterior mediastinum." He therefore proved that the so-called oat cell sarcoma of the posterior mediastinum was in reality a carcinoma of the bronchus. This milestone in the history of bronchogenic carcinoma is of great importance, for it was after this time that bronchogenic carcinomata which were so far missed were correctly diagnosed in the autopsy room. Many enthusiastic workers of the autopsy room were not only satisfied with avoiding the mistake after that, but they re-examined the old specimens and sections and corrected many a false label.

Naked eye three main types and several other modifications have been described. The differentiation depends upon the situation and the nature of the growth. Thus we have—

- (1) Hilus carcinoma
- (2) Diffuse carcinoma or carcinomatous pneumonia or lobar carcinoma
- (3) Millary carcinoma or lymphangitis carcinomatosa
- (4) Interlobar carcinomatous nodule
- (5) Purely intra-bronchial carcinoma or malignant adenoma of the lung

Almost all these terms are self-explanatory I will not deal with them but I wish to draw your attention to the last named condition known as the malignant adenoma of the lung which was first fully described by Hampert in 1937 and later on by Womach and Graham (1938), Goldman (1940), Brunn and Goldman (1940) and by Adams, Steiner and Bach in 1942 These tumours start invariably in the primary or the secondary bronchi as benign polypoid adenomas which are purely intrabronchial but later penetrate the wall of the bronchus Metastasis may occur after a period of five to eight years These tumours are definitely malignant but the malignancy is of a low grade

Microscopically the tumours are divided into three main groups, viz, squamous carcinoma, adenocarcinoma and the small cell carcinoma or the oat cell carcinoma The importance of this histological classification to the clinician is stressed by Simon Koletsky who believes that "the histological classification of primary bronchogenic carcinoma can be co-related with essential difference in the growth, dissemination, clinical course and prognosis of each type of the tumour"

The squamous type is usually hilar, starting in the primary or the secondary bronchi and occurring in slightly older people (Davidson), such a tumour is less rapid in its growth and passes through the following stages, viz, (i) hypertrophy, hyperplasia and protoplasia of the bronchial mucosa—carcinoma in situ, (ii) occlusion of the bronchus of a varying degree, (iii) extension along the bronchial wall causing fibrosis, (iv) lymphatic involvement, and lastly, (v) distal metastasis In the adenocarcinoma the spread is by the blood and hence fairly rapid. The small or the oat cell type arises in the third or the fourth bronchus of Foster-Carter and spreads very rapidly by the blood stream as well as the lymph stream

The relative frequency with which each one of these types occurs is not very definite and figures worked out by Brindley, Koletsky and Hill are given in Table 5

Table 5 Relative Incidence of Histological types

Author	Total No of cases	Squamous	Small cell	Adenocarcinoma
Brindley	90	49	1	40
Koletsky	97	40	35	22
Hill	513	20%	50%	30%

*Site of origin*—It has been found that whether the tumour originates in the right lung or the left lung and in the upper or the middle or the lower lobe is of no particular importance to the clinician because it does not influence the clinical course, prognosis or the treatment in any way The distribution is almost equal in both the lungs because the irritant agent is mostly air-borne and volatile and therefore affects both the lungs almost equally The figures of the various authors have been collected in Table 6



Table 6 Site of Origin

Author	Total No	Right	Left
Menn & Anderson (collected from others)	117	51 %	40 %
Brindley	99	46	44
Koletsky	97 (4 bilateral)	54	39
Singer	3735	55 %	45 %
Ochsner & De Bakey (Collected from literature)	4732	58 %	42 %

**Clinical Picture**—Time and again attempts have been made to find a definite sign or symptom or a set clinical pattern which would enable an observer to make an early diagnosis of a case of bronchogenic carcinoma but with each attempt we seem to recede farther from a well defined syndrome and the picture becomes more and more bizarre. The reason for this is not far to seek because there is not a single symptom or sign which is characteristic of the carcinoma itself, all such being produced by the underlying morbid anatomy which not only may be different in different cases of bronchogenic carcinoma but may also be simulated by any inflammatory lesion of the respiratory tract and depend essentially on the location and the size of the growth.

**Symptoms**—The symptoms presented by a bronchogenic carcinoma may be divided for the purpose of description into three groups, viz., (1) local or respiratory symptoms, (2) general or constitutional symptoms, (3) symptoms of extension or metastasis and any one or more groups of symptoms may be present in a given case. In as many as 5 per cent of cases there are not to be found any symptoms referable to respiratory tract disease and the diagnosis may be missed if the condition is not thought of.

**Local Symptoms**—Cough is an early symptom found in a majority of cases. Tinney found it in as many as 81 per cent of cases in a series of 448 cases. To start with it is dry unproductive cough and is often mistaken by the patient and the clinician for cigarette cough. Expectoration occurs only when the tumour is sufficiently large enough to cause partial obstruction of the bronchus and retention of the secretions.

Pain in the chest is present in almost half the number of cases and may range from a mild discomfort to sharp shooting pain. This is a very important symptom even when no other signs are present. In the absence of definite signs of pleurisy, severe chest pain with or without vague pulmonary signs should not be neglected until a pulmonary malignancy is ruled out (Singer). Severe pain always suggests that the lesion is spreading to the mediastinum or the thoracic wall and pleura and therefore less easily available to the surgeon. Usually pain is the first symptom when the bronchogenic carcinoma originates at the apex of a lung—the so-called Pancoast tumour (1932). This is due to involvement of the brachial nerves and the pain may shoot down along the arm. Talking of these vague chest pains Marloo quotes nine cases which were referred to him for psychological treatment following a diagnosis of neurosis, which later on proved to be cases of bronchogenic carcinoma. He summarises that

"pain in the right arm and chest with or without hyperaesthesia in the affected area, with increased or diminished tendon jerks and a definitely high erythrocyte sedimentation rate suggests so strongly a bronchogenic carcinoma that even a negative radiogram should not be relied upon until all the other special investigations have been done. In absence of a thorough examination of this type many such cases supposed to be functional, die of pulmonary malignancy without even a suspicion of pulmonary disease being raised" (Marloo). It becomes all the more important that such cases be investigated thoroughly and detected as early as possible, when we know that only in the early stages is the disease definitely amenable to treatment. This makes the delay and neglect all the more unpardonable.

Rarely, as in one case cited by Singer, the pain is spoken of by the patient as a mere precordial distress.

Dyspnoea is a fairly frequent symptom but comes a little late in the course of the disease unless there is some complication like a sudden development of atelectasis or block or the rapid development of pleural effusion, otherwise the patients complain of "repeated chest colds" only. The importance of dyspnoea was recognised as early as 1926 by Fishberg who remarked that "it is important to think of pulmonary neoplasm, when a patient in the cancer age, showing no symptoms of cardiac, renal or arterial disease begins to cough and is short-winded."

Haemoptysis, though not uncommon at one time or other during the course of a bronchogenic carcinoma, is rarely found in the beginning. The blood in the sputum may be just enough to cause a streaking of the sputum or the loss may be in a quantity sufficient to bring about a fatal termination.

Hoarseness of voice is due to involvement of the recurrent laryngeal nerve and is found in a few cases.

*General Symptoms*—The usual symptoms of a disease anywhere in the body are also found in this condition and the patients complain of undue fatigability, weakness, night sweats, anorexia, etc., but the most striking feature is the loss of weight. The loss though constantly present, is by no means an early feature of the disease and in the beginning there may even be a gain of few pounds as in ovarian tumours. When the obstruction to a bronchus becomes sufficient to cause retention of secretion it is likely to be secondarily infected giving rise to chills and fever.

*Symptoms of Extension or Metastasis*—These usually come late in the course of the disease and are least observable in the squamous type of growth whereas they are fairly frequent and come early in the small cell and the adenocarcinomatous types. Such symptoms may vary from vague backache, abdominal pain and vomiting to slight or profuse haematuria, dysphagia, shooting root pains and complete paraplegia.

The chief complaint makes its appearance, depending upon the type of growth, about 1 to 15 months before death, the patient usually seeking medical advice late in the course of disease, usually for hae-

moptysis, loss of weight or dissemination symptoms The duration of symptoms as worked out by Simon Koletsky, on an average, is six months for a small cell carcinoma, eight months for an adenocarcinoma and twelve to fifteen months for a squamous carcinoma

Table 7 Relative frequency of symptoms

Symptom		Tinney in %	Authors Singer No of cases
Local	Cough	81%	17
	Expectoration	70%	10
	Haemoptysis	58%	6
	Pain in chest	54%	11
	Dyspnoea		11
	Hoarseness of voice		8
General	Loss of weight	71%	0
	Fever & Chill	50%	10
Extension	Nervous		8
	Vague backache		7
	Urinary		3
	Vomiting	Not quoted	2
	Abdominal pain		1
	Enlarged abdomen, Dysphagia		1
Total No of cases seen		448	26

The various clinical signs produced by bronchogenic carcinoma depend upon (1) the size of the tumour, (2) degree of obstruction produced, (3) extent of infection in retained secretion, and (4) the presence of metastasis Over and above the signs of respiratory diseases like pneumonia, bronchitis, bronchiectasis, lung abscess, pleural effusion, collapse of the lung and pulmonary tuberculosis there may be the presence of enlarged, hard and fixed lymph nodes in the supraclavicular fossa or even in the axilla The signs may also resemble an aneurysm of the aorta The physical signs are not of the disease entity but of the underlying morbid anatomy and as such they can only lead to a suspicion and cannot be of a diagnostic nature unless some metastasis or other makes its appearance, or one of the specialised investigations yields a positive result In Tinney's series of 448 cases at the Mayo Clinic, signs of bronchitis were found in 12 per cent of cases and effusion in 15 per cent The clinical picture resembled pulmonary tuberculosis in 3 per cent of his series

*Metastasis*—These are most common in the small cell and the adenocarcinoma and least often found in the squamous carcinoma The metastasis are commonly found in the lymph nodes, liver, adrenals, brain, other lung, kidneys and spine but may also be deposited in the pancreas, skin, spleen, heart and the thyroid The figures of Koletsky and Tinney are given below in Table 8

Table 8 Relative frequency of Metastasis

Metastasis	Authors	
	Koletsky %	Tinney %
Lymph nodes	61%	70%
Liver	40	34
Adrenals	38	36
Brain	22	19
Kidneys	21	21

Other lung	21	49
Spine	10	
Pancreas	18	
Skin	11	
Spleen	11	
Heart	7	19
Thyroid	4	

In my selected cases there has been a metastasis in every one of the possible places mentioned by Koletsky

Quite a number of times bronchogenic carcinoma may be superimposed on an already diseased lung. In Koletsky's series of 97 cases he found besides bronchogenic carcinoma pulmonary tuberculosis, pneumokoniosis and pulmonary suppuration in 21 cases as shown in Table 9

Table 9.—Associated lung diseases

Disease	No. of cases
Active Tuberculosis	3
Old Tuberculosis	5
Pneumokoniosis	5
Pulm. suppuration	8

**Diagnosis**—The importance of any paper on bronchogenic carcinoma depends upon the help it renders in the early diagnosis of a case. At the end of the first decade of the twentieth century when Alder published his 374 cases of bronchogenic carcinoma collected from the literature the ante-mortem diagnosis was successfully made in not more than 2 per cent of cases. By the end of the second decade the position had been improved to some extent and 20 per cent of cases were spotted by the clinician. In Koletsky's series of 97 cases published in 1937 56 per cent of cases had been correctly diagnosed by the clinician and in 1940 this figure has been raised to 75 to 90 per cent in well equipped institutions like the Mayo Clinic where the different specialist units work in close corroboration for the diagnosis and treatment of every case. The difficulty and delay in diagnosis may be ascribed to causes like absence of a specific syndrome and scarcity of the modern methods of diagnosis but above all due to the complacent attitude of the clinician who still considers the condition to be relatively rare. It seems that there is only one method, only one way to arrive at an early diagnosis of bronchogenic carcinoma and that is to think of it, to suspect it, in every case with respiratory signs and symptoms which cannot be easily explained away and not to rest, till the case is satisfactorily proved to be otherwise, by all the modern methods of diagnosis at our command. It is with this aim in view that more space has been allotted to a detailed discussion of the various methods of diagnosis.

(a) **History**—As in the diagnosis of any other condition history is of prime importance. It should be taken in a chronological order and repeated attacks of "weak chest" or "chest colds" should be enough to arouse suspicion. No amount of laboratory aid can entirely substitute a well taken clinical history.

(b) *Physical Examination* is the next step and besides the routine examination of heart, lungs and nervous system special attention must be paid to the examination of cervical and axillary lymph nodes, the trachea and the mediastinum, and the bones and skin should be examined for evidences of small secondary deposits

(c) Next comes the examination of blood wherein a high sedimentation rate in absence of any evident cause is always highly suggestive. Moersch found the erythrocyte sedimentation rate more than 30 mm per hour by Westergreen's method in 88 per cent of cases

(d) Examination of sputum by the specialised Dudgeon and Wrigly's method when done by an experienced histopathologist helps in making a diagnosis in about 60 per cent of cases. Prof Leonard Dudgeon and Dr C H Wrigly could demonstrate the presence of malignant cells in 26 out of 38 cases of malignancy of the respiratory tract. Of these 38 cases, one was of a secondary carcinoma and 3 were cases of carcinoma of the larynx. Not only could they make a diagnosis of the presence of malignancy but in as many as 20 out of these 26 cases they could also tell the histology and the type of the tumour by mere sputum examination. Though this method of examining the sputum was described by Prof Dudgeon as late as 1935, Betschart described 4 cases of malignancy of lung, as early as 1895, where he found that "pieces of tumour tissue were expectorated out, and in two cases the pieces were 5 cm long and 2 cm long". Others like Hamplen (1919) and Sweany (1934) have from time to time described cases where malignant cells were found in the sputum. As late as 1934, Hill described 513 cases of malignancy of the lung of which 47 per cent had blood in the sputum and he suggested that "malignant tissue may rarely be expectorated out" though he could quote no examples himself. The difficulty in examination of sputum arises in cases of acute inflammatory conditions of the respiratory tract, as was found by Dudgeon and Wrigly who reported a case of acute sinusitis as positive, and also in examination of expectorated tissues which have undergone autolysis after expectoration. In order to avoid autolysis and digestion by the polymorphonuclear leucocytes a fresh specimen is taken and a wet film is made of the blood streaked portion or the solid portion. This is immediately fixed in Schaudinn's fluid for 20 minutes, washed in methylated spirit and tincture of iodine and then washed in distilled water. The film is then stained with Mayer's haemalum for 2 minutes or even less, so as to avoid deep staining. It is then washed in tap water till "blueing" of the film occurs. Then it is counterstained with weak eosin, washed in alcohol and fixed in xylol and Canada balsam and examined for malignant cells with hyperchromatic nuclei and mitotic figures. The usual routine is to prepare six slides from every specimen and on an average about twelve specimens are seen before a negative result is given.

Sometimes even by ordinary methods of examination of sputum with eosin and methylene blue the malignant cells can be seen but the proportion of such cases is extremely small.

(e) If there is a pleural effusion, the fluid should be tapped and a routine examination should be made. The fluid may be haemorrhagic if the growth is subpleural but it may as well or perhaps more often be the simple exudate such as is found in tubercular pleurisy. Examination of fluid for malignant cells by Mandelbaum's method, —i.e., centrifuging the fluid and fixing deposit like a tissue—should be carried out to look for malignant cells.

(f) Next comes a plain roentgenogram. In Moersch's series of 448 cases 72 per cent were diagnosed radiologically. Kirklin divides the positive radiological evidence of bronchogenic carcinoma into 3 groups, viz.,

- (1) Where the tumour itself casts a distinct shadow
- (2) Where secondary manifestations are prominent, e.g., rarefaction of ribs, fracture of ribs or atelectasis of lung
- (3) Where some complication is more prominent than the tumour shadow, e.g., lung abscess and pleural effusion. In such a case the effusion should be completely removed and the lung allowed to expand and a radiogram should be immediately taken to see if the tumour shadow is seen in the expanded lung. A contrast picture after air replacement should also be taken to detect malignancy of pleura or subpleural structures.

At times a bronchogenic carcinoma may yield a bizarre picture which is difficult to interpret.

A negative plain film does by no means rule out the possibility of a bronchogenic carcinoma. If a plain P.A. film of chest at 2M is negative, a lateral view should be taken. If even this is normal then specialised procedures like radiotomy or body-section radiography introduced by Bocage in 1938 should be tried. This consists of properly co-ordinating the movements of the X-ray tube and the film during the exposure in such a way that a predetermined layer in the body is radiographed with the exclusion of the structure lying in front of or behind the predetermined layer (Sherwood Moore).

A bronchogram after iodized oil may help in showing the early obstruction in one of the main bronchi when the obstruction is not sufficient enough to cause atelectasis.

(g) Bronchoscopy is another important item in our diagnostic armamentarium which may also be of therapeutic use. The bronchoscope can diagnose as many as 70 to 75 per cent (Moersch) of tumours the rest being outside the reach of the bronchoscope. The appearance of the tumour may be from a small thickening of the mucosa, invisible to any but the most experienced eye, to a fair sized polypoidal mass. A section should always be taken to determine the nature and character of the growth and its operability.

(h) If all these procedures fail to reveal the presence and the nature of the growth, thoracoscopy and biopsy of lungs and pleura by a thick bore needle or even an exploratory thoractomy may have to be done.

Table 10.—Mode of Diagnosis (Craver)

Mode of diagnosis	No. of cases
Bronchoscopy	80
Aspiration biopsy	63
Autopsy	15
Thoracotomy	8
Biopsy of lymph nodes	7
Expectorated tissue	2
Total	175

Table 11.—Mistakes in diagnosis (Koletsky)

Diagnosis	No. of cases
Lung abscess	9
Pulmonary tuberculosis	9
Pleural effusion	1
Encephalomalacia	1
Carcinoma unknown	4
Stomach	4
Thyroid	1
Prostate	1
Kidney	1
Oesophagus	1
Mediastinal Sarcoma	2
N Y D	10
Total	44

*Differential Diagnosis*—The most important differential diagnosis is from the other lung conditions, which are secondary to the growth but which may be taken as the primary disease. The other liability to error is to determine the site of the primary malignant disease. At times the disease may not be diagnosed at all and the diagnosis may remain a mystery till cleared by an autopsy. In Simon Koletsky's series of 97 cases 44 were misdiagnosed as shown in Table 11.

*Prognosis*—As mentioned in the beginning of this paper the dark clouds of despair and helplessness are showing a bright silver lining and quite a broad lining at that. The disease which only a score of years ago spelled sure death within a year to its unfortunate victim can now be conquered provided it is detected early enough. The prognosis is most hopeful in case of a squamous carcinoma and least so with a quickly disseminating small cell carcinoma. The prognosis darkens with every day lost before commencement of effective treatment and is helpless once metastases appear even in spite of radiotherapy.

*Treatment*—"Serious diseases have serious remedies" is an old Arabic proverb and it is nowhere more true than in the case of pulmonary malignancy. The treatment of bronchogenic carcinoma, if accessible, is complete excision of the affected lung. The operation is a formidable one and presents four problems to the surgeon, viz, (1) What is to be done with the empty space, (2) Closure of the thick and calcified bronchus, (3) Tying of the fragile and short pulmonary vessels, (4) The late effects on the heart and the other lung. In spite of these dangers and the considerable risk involved, pneumonectomy seems to be the ideal treatment and is preferable to radium or deep X-rays, (Brindley Jr). The farther away a tumour is from the mediastinum, the lesser is the probability of invasion of mediastinum and the lighter is the surgeon's job. In the past electro-coagulation of a growth accessible through the bronchoscope and a bronchoscopic implantation of radon and radium in the growth have been tried but none of these methods have succeeded in bringing about the 5 years cure. Ochsner and DeBailey suggest that total removal of the involved lung and the mediastinal lymph nodes is the most rational surgical procedure whenever possible and that it should be performed by individual ligation of the hilar structures. They condemn the use of the pulmonary noose tourniquet for malignant cases. They record

a recovery rate of 40 per cent Churchill on the other hand, could succeed in saving only 5 cases out of the 27 subjected to pneumonectomy, the other 22 dying in the hospital or just a little after. He therefore advocates an early diagnosis and lobectomy, before the mediastinal involvement, because of the considerably lowered operative risk. Brindley records 43 complete pneumonectomies with removal of mediastinal lymph nodes performed at the Mayo Clinic from 1925 to 1943 for bronchogenic carcinoma. Of these 43 cases, 4 could not be traced, 12 died in the hospital, 1 died 3 months later, and 1 had recurrence of pleural malignancy 9 months after. Of the remaining 25 patients, 9 are known to be healthy without known recurrence for 1 to 6 months, 6 for 7 to 12 months, 5 for 13 to 18 months, 1 for 19 to 24 months, 3 for 24 to 30 months and 1 for 48 months.

If lasting benefit is what is aimed at, and not mere temporary abatement of symptoms, total and radical pneumonectomy whenever possible is the only treatment for a patient of bronchogenic carcinoma. In expert hands and with selected cases the mortality is as low as 15 per cent, and with early diagnosis, improvements in anaesthesia, surgical technique and pre- and post-operative care and with a wholehearted and greater collaboration between the clinician, the pathologist, the bronchoscopist, the radiologist and the surgeon's team there is every hope that this figure will be reduced still further.

## SUMMARY

- (1) 8 cases of Bronchogenic Carcinoma are described to illustrate the diversity of its clinical picture
- (2) The available literature on the subject is reviewed
- (3) A plea is made to think of bronchogenic carcinoma in all cases of vague respiratory symptoms which cannot be definitely accounted for and in all cases of obscure cerebral, nervous, or other symptoms which may suggest the possibility of widespread metastases.

(My thanks are due to the Dean, K. E. M. Hospital for, permission to use the Hospital records and to my chiefs Dr N. D. Patel and Dr P. Raghavan, for the encouragement and facilities they gave me in my work.)

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## DISCUSSION

**Dr Z J Joseph** spoke on the Radiological Features of Primary Carcinoma of the Lung

He said "These may be classified as (1) **Hilar Carcinoma** and (2) **Lobar Carcinoma**. **Hilar Carcinoma** starts usually as an endobronchial tumour. This cannot be seen in a plain X-ray film and endoscopy is often required. This growth can be directly demonstrated by bronchography. The Lipiodol injection shows irregularity and narrowing of the lumen or obstruction with the rat tailed tapering at the site of the growth. Extension of the growth takes place by local infiltration or along the lymphatics. This growth may produce blocking of the bronchus, either by growing inside the bronchus, or by gradual compression by the growth from without. Secondary atelectasis of a lobe, or the whole lung may take place. This atelectasis comes on gradually but sometimes may be rapid. Atelectasis produces opacity of that lobe, or opacity of the whole side of the chest if that whole lung is collapsed. The diaphragm on that side is raised, the heart, aorta and the mediastinum are pulled to the side of the growth. **Lobar Carcinoma** arises from small bronchus in the lung parenchyma, penetrates the bronchial wall and often grows as a rounded nodule, preserving a well defined outline, until it reaches a considerable size."

**Dr J C Paymaster** said "Out of a total of 7,000 cancer cases seen at the Tata Memorial Hospital, Bombay, there were 118 lung problems recorded. Out of these 70 cases have been diagnosed as primary cancer of the lung with fair amount of accuracy from the physical examination, X-ray pictures and in over half the number of cases from the biopsy."

There were 66 males and 4 females. The youngest patient was 25 years and the oldest was 72 years of age, the average age recorded being 48 years.

Pain in the diseased side of the chest and cough were the main symptoms recorded in 56 cases.

The right lung was affected in 40 cases and the left lung in 30 cases.

In 37 cases there was positive histological evidence which was obtained as follows —

- 15 cases had aspiration biopsy from the lung tumour
- 1 case had a smear made from the centrifuged deposit of the pleural fluid
- 6 cases had biopsy performed through the bronchoscope
- 6 cases had aspiration biopsy from the lymph nodes either from the neck or the axilla
- 5 cases excision of the node
- 1 case had lobectomy performed for the cancer
- 3 cases had post mortem performed

Most of these cases came quite late, low and run-down in health, as seen from 9 cases which expired in the hospital within a fortnight of admission without any treatment.

The treatment of choice for a suitable early case of cancer of the lung is pneumonectomy, radiation being only a palliative

**Dr K. P Mody** in the course of the discussion stressed the importance of the subject, as the incidence of the disease had increased considerably during recent years. One of the most valuable method of diagnosing the condition was X-rays, but he felt that this was neither simple nor straightforward as X-ray appearances were varied and were complicated by secondary pathological changes due to infection. It was most important to diagnose the condition in the early stage and this was particularly difficult as there were hardly any early symptoms. At this stage of the disease bronchoscopy and bronchography were of immense value, and he congratulated **Dr Joseph** on this excellent demonstration of an early case in which lipiodol injection showed up a small filling defect in the bronchus. Obviously the only chance of a successful cure was in this stage of localised growth. It ought to be laid down as a dictum that any case of a cough which could not be explained by the usual causes should be thoroughly investigated by bronchoscopy, bronchography, tomography and routine X-ray examination.

He agreed that the only chance of successful cure was by radical surgery. Unfortunately the field of selection was very limited. Out of 100 cases only 15 were suitable for such drastic treatment. The mortality was 50 per cent for pneumonectomy, so that very few cases could be salvaged. Radiation treatment offered hardly any prospects of a cure, though stray cases have been reported of 5 years' and 7 years' survival. Palliation was possible and the patient made more comfortable.

Discussing the technique of radiation treatment, the important factors were small daily doses, high voltage and small fields accurately centred on the lesion. The total dose had to be heavy the treatment lasted from 45 to 60 days, so that the dose received by the tumour was at least 3,500 units. Supervoltage therapy would be ideal for such deep seated lesions.

**Dr S N Kothare** gave a brief review of seven cases of bronchial carcinoma autopsied during the years 1943, 1944 and 1945. He said

"All these seven cases were of hilar type, the right bronchus was involved more often than the left.

"Histologically five of these were spheroidal type, one of squamous and one of adenocarcinoma of bronchial mucous membrane. In these cases as well as those reported by **Dr L Montelero** two years ago, the spheroidal type was more common than the squamous as opposed to foreign publications in which the incidence of the latter type was much higher. As regards the sex incidence it seemed to be more common in males, six of these being males. The number of autopsies performed on female bodies will have to be taken into consideration to judge the sex incidence correctly.

The importance of frequent metastases of bronchial carcinoma in adrenals and brains was stressed and their involvement being taken

as a guide in autopsy room, especially when the primary is very small and the secondaries are many and large "

**Dr H D Gandhi** said that the place of pride for diagnosis of bronchial carcinoma should go to the bronchoscopist because it is in the bronchial tree that the growth arises. The growth is demonstrable to the naked eye, its extent can be made out and biopsy taken. In this way early cases can be detected. Cough is a very early and very constant symptom of bronchial cancer. Hence it should be the practice of all internists, in all cases of intractable cough, after tuberculosis has been excluded, to make an attempt to find the cause by routine bronchoscopy.

**Dr N K. Sahar** stressed the difficulty in diagnosis of cases showing extra-pulmonary metastasis. In this connection he mentioned one of his cases who was unconscious and showed glycosuria, a condition mistaken for diabetic coma. The diagnosis at the autopsy was a bronchial carcinoma with metastasis in the brain.

**Dr V R Khanolkar** in concluding the evening's proceedings congratulated Dr Motashaw on the very painstaking and exhaustive presentation of the subject. The discussion which followed had brought into relief certain important aspects of the subject. There was therefore very little to add, except to mention a few stray observations. Dr Khanolkar said that he became particularly interested in lung cancer, after hearing the lucid discourses on the subject by Erdheim in Vienna where he had the privilege of working 10 years ago. Curiously enough, carcinoma of the lung was recorded as a definite clinical entity relatively recently. It was in 1855 that Bayle had separated a group of pthisis as cancerous and had described its main characteristics. Probably the most vivid description of a case of lung cancer was given by the famous anatomist Boerhaave who had watched a French nobleman, le marquis de Saint-Armand for two years and had finally performed an autopsy on him. As regards the incidence of lung cancer, Erdheim in Vienna used to teach that the disease was seen not only more frequently in Europe in recent years but was also changing its type. It was found more often in younger persons and presented slightly different clinical manifestations. Dr Khanolkar stated that his experience of last 20 years based on an autopsy material of the K.E.M. Hospital and the clinical material at the Tata Memorial Hospital showed that lung cancer did not occupy the same important position in Bombay as it did in Europe and U.S.A. There was a difference in the type incidence also so that the oat-cell type which seemed to be the commonest variety in England was seen rarely in Bombay as compared to the squamous cell and the adenocarcinoma. The metastatic spread of lung cancer presented peculiarities which deserved particular mention. The lung cancer appeared to have a definite predilection to metastasize in the brain and the suprarenals (Dosquet).<sup>1</sup> Dr Kothare's observations therefore had special interest in this connection. Fried and Buckley,<sup>2</sup> had observed that cancer of the lung yielded brain metastases in

as many as 41 per cent of their cases. The histological variety which gave the largest number of such secondaries was the adenocarcinoma. Dr Sahlar had no reason to be chagrined about the mistaken diagnosis in these cases, as it has been pointed out by Willis,<sup>3</sup> "So frequent are diagnostic errors and so protean that in all cases of seemingly primary nervous disorder the possibility of the existence of a latent pulmonary neoplasm demands serious consideration." Dr Khanolkar mentioned that he had assisted at two autopsies, one in Vienna and another in Prague where very reputed surgeons had operated on the brain in cases of alleged cerebral tumours and it was later discovered that the primary growth was a very small bronchial carcinoma. Another peculiarity in the spread of lung cancer had recently puzzled the staff of Tata Memorial Hospital, Bombay and was worthy of notice. The lymph nodes which were usually involved in lung cancer were the intertracheo-bronchial and the inter-bronchial nodes situated in the mediastinum and at the hilum. It was well known that a voluminous enlargement of some of these nodes could take place without a microscopic involvement of the intervening lymphatic tissue. The interesting spread however was in the nodes in the supraclavicular fossa and in the axilla. They had recently come across patients whose only complaint appeared to be a swelling in the lower neck or in the arm pit, and it was only a very careful clinical and radiological investigation which had revealed a primary cancerous lesion in the lung. It had to be pointed out that about 10 years ago the French anatomist Rouviere had insisted on the existence of a direct lymph route which joined the parietal pleura with these two regions. He had pointed out that some lymph from the pleura of the apical region and the uppermost portion of the superior lobe drained into the supraclavicular fossa, and that the lymphatics of the interlobar and the upper portion of the lower lobe led into the axilla. The evolution of the tumours often diagnosed as Pancoast's tumour could be probably explained on the basis of this anatomical peculiarity in the lymph drainage.

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# TOTAL LARYNGECTOMY

## A SIMPLE DEVICE FOR VOICE PRODUCTION

by

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The question of voice production after laryngectomy has engaged the attention of surgeons since Billroth performed the first laryngectomy for carcinoma of the larynx. Total laryngectomy is in itself a formidable procedure added to which the patient has to face the ordeal of going through life quite voiceless. All patients necessarily feel this handicap very much. At first the patient tries to make up for the loss of voice by attracting attention by clapping hands and making characteristic gestures. In the earlier days a slate and pencil are his only means of conveying to others his wants.

As time goes on some patients may attempt a form of speech which is just an audible whisper or if trained may actually produce a serviceably loud enough pharyngeal voice to carry on their normal vocation in life. Most of the patients have to go through life without speech unless an artificial larynx is fitted on.

Chiloff studying the voice production after laryngectomy has shown that the reservoir of air is in the lower part of the stomach and oesophagus, this air is swallowed and its expulsion through the pharynx can bring about vibration of a pseudo-glottis which probably corresponds to the upper edges of the middle constrictor.

Patients could therefore be trained to speak without artificial aids and cases are recorded where patients were able to speak almost as well as when their larynx was intact. This method of speech however entails a very great effort on the part of the patient who must be both intelligent and industrious and it taxes the ingenuity of the surgeon to the utmost. In the average hospital class of patient it would be next to impossible to attempt to teach the patients the use of a pharyngeal voice.

To obviate such difficulties various instruments, both simple and complicated, are designed to enable the patient, deprived of voice, to speak. The instruments in use are those of Tapia and Mackenty, the latter perfected by the Western Electric Co., is the most serviceable and has a pitch regulating device. Unfortunately at the present time these instruments are very difficult to obtain in India. Another adverse consideration is their cost which is not within the reach of the average patient of the hospital class.

Necessity if nothing else compelled me to attempt to produce an apparatus which would be cheap and yet effective. The first attempt in voice production with the simple apparatus about to be described was made on a patient on whom a total laryngectomy was done by Dr Homi Gandhi at the K. E. M. Hospital, Bombay, and was very eager to have an artificial larynx.

The apparatus consisted of two rubber tubings hard in consistency and each about six inches in length. The proximal end of one tube was fitted into the tracheotomy tube by means of a metal adaptor. The distal end of the first tube was adapted to an ordinary bamboo reed (the type which is sold at any street corner, usually fixed inside toy flutes). The distal end of the reed was attached to the proximal end of the second rubber tubing the other end of which went to the mouth to enable the patient to breathe easily and without producing a sound, when a sound was required to be produced the patient had only to close the opening with his thumb and breathe through the reed. This simple device enabled the patient to articulate freely, to his great surprise and delight. There was however one great difficulty with this bamboo reed viz that within less than twenty-four hours it would get sodden and useless for any voice production.



Figures 1, 2, and 3

The difficulty of getting a more lasting and useful sound-box seemed now insurmountable. The bamboo reed was an adequate sound-box but was not practicable as it was so easily put out of gear.

To obviate this difficulty I substituted a tuning pipe for the bamboo reed. These tuning pipes which are sold at any musical dealers are small metal cylinders with a vibrating reed inside them, they are available in four notes E.A.D.G. and depending on the pitch of the voice desired one of these is used, the most suitable being A. The patient could use this tuning pipe with much less effort than the original bamboo reed that I first used and more important, it stood wear and tear for about a year without deterioration.

A slight modification to the original model has been made by the patient himself who made a silver adaptor with a hole on its superior

aspect so that it obviates the necessity of cutting a hole in the rubber tubing

The patient on whom this apparatus was fitted was very intelligent and was able to talk quite fluently within a week of fitting the apparatus. He spoke recently at the All India Surgical Conference at Lucknow where the artificial larynx was demonstrated.

Of course the use of the apparatus does need a little effort but with a little patience and perseverance, any man should be able to express himself perfectly well.

The great advantage of this instrument is that it is very cheap and hence within the reach of any hospital class of patient, the whole apparatus could be rigged up for the price of about one rupee.

The apparatus has nothing new in principle. The theme is old but its application has been varied to suit not only circumstances but our purses. Where Mackenty's instrument has an elaborate sound-box this instrument has just a solitary tuning pipe for a sound-box.

The one disadvantage the instrument has is that it produces a constantly monotonous sound. The alteration in this monotony is a problem to be followed up and improved.

My thanks are due to Dr. H. D. Gandhi for allowing me to publish this work done by me with his guidance and inspiration.

## Book Reviews and Notices

**Year Book of General Therapeutics, 1944** Edited by Bethen. The Year Book Publishers 304 South Dearborn Street Chicago Pp 447 Price \$ 3 00

The year books published from Chicago have successfully solved for the busy practitioner the problem of keeping himself acquainted with the ever-increasing number of papers appearing in medical periodicals. The volumes are handy and well printed, the articles are critically chosen, well written and judiciously commented on.

The Year Book of Therapeutics, 1944, reflects the trend of therapeutic advances during the previous year. Some 55 pages are devoted to articles dealing with sulfonamides, some 60 pages to articles dealing with penicillin, 10 pages to Antimalarials, and 50 pages to hormones and vitamins.

There are interesting articles about newer drugs such as Demenol, Neostigmine, Depropane, Dicumarol, Heparin, Thiouracil, Ethylene disulphonate, Avidin etc. There is a detailed account of the use of gamma globulin in measles and a clear account of the Rh factor in transfusion. Many useful articles on transfusions and infusions, and on newer therapeutic techniques are also included.

The articles dealing with details of treatment are all practical and we have no hesitation in confidently recommending this useful book to general practitioners.

**Year Book of Neurology, Psychiatry and Endocrinology, 1944**, Edited by Reese Lewis and Sevringhaus. The Year Book Publishers, 304, South Dearborn Street, Chicago Pp 712 Price \$ 8 00

The Year Book of Neurology, Psychiatry, and Endocrinology, 1944, maintains the usual features characteristic of these excellent man-

nuals The section of Neurology contains an interesting article on Headache mechanisms and differential diagnosis by Wolff In the treatment of migraine, Meniere's syndrome and some headaches the value of salt mixture of Pfeiffer, calcium lactate and potassium chloride (3 1), is stressed The mechanism of these states is thought to be in a vascular dysfunction and the correction is attempted by histamine, nicotinic acid, potassium and calcium mixture, or a salt-free diet The articles on meningitis give a timely warning on the indiscriminate use of intraspinal therapy which, to say the least, is unphysiologic Sulphadiazine continues to be the drug of choice for meningococcal disease Combined penicillin and sulphonamide therapy has produced encouraging results in pneumococcal meningitis

In the section on Psychiatry there are many articles dealing with the present position of Shock therapy in mental disorders An abstract on shock narcosis is suggestive Attention is drawn to psychoses due to commonly used drugs such as bromides, sulphonamides, and barbiturates

The practice of clinical endocrinology in India is in a state of chaos Few practitioners know what they are prescribing and why It is a hit-and-miss business Advertiser's circulars are hastily looked at and some potent and many useless preparations are hopefully handed out to patients even before any definite diagnosis is made From the procedure, the only person to benefit is the manufacturer, the patient usually suffers more, and the doctor's confused mind gets more confounded There is a great need for an authoritative text on clinical endocrinology In the absence of such a text, the practitioner who desires, a rational basis for hormonal therapy,—always in a fluid state,—can do worse than refer to Sevringhaus's annual abstracts in the Year Book

**Penicillin Therapy** by J R Goyal, M.B.B.S., New Delhi published by B. Dutta, Esq. Manager The Albion Press Kashmir Gate, Delhi Pp 148, price Rs 5/ To be had from the Medical Review of Reviews P.O. Box 160, Delhi

**Penicillin**—The discovery and development of, published and distributed gratis by Imperial Chemical (Pharmaceuticals) Ltd., and Therapeutic Research Corporation of Great Britain Ltd

**Penicillin**—A collection 28 articles reprinted from various journals by the United States Office of War Information and distributed gratis

Dr Goyal's booklet summarises the present position of penicillin therapy, in a way likely to be useful to the general practitioner We do not agree with Dr Goyal's statement that penicillin is effective in meningococcal infection and that it should be administered by intrathecal or intracisternal routes (p 46) The use of penicillin intrathecally is highly irritant Its use intraventricularly has produced collapse of circulation and convulsions The method is unphysiologic Again, Sylvester and Rosenberg (Science, 100 132-133 Aug 11, 1944) have demonstrated that after intravenous or intramuscular injection of penicillin, in doses of 20,000-40,000 oxford units, the concentration of the drug in the spinal fluid was adequate to control meningitis However, in severe pneumococcal meningitis intrathecal penicillin, 1000 units per 1 c.c., 10,000 units once or twice a day, is to be recommended

Any practitioner who acquires these three booklets will get all the information he needs for the rational use of penicillin in his practice



## Reflections & Aphorisms

—"The physician of today must be the medical historian of each of his patients, directing particular attention toward discovering the first causes and developments of the illness      Medicine cannot remain equal to its great task without preserving for the physician his double character of scientist and worker for the people    If in the exercise of his art he is guided by his knowledge of the laws of nature, then his technical knowledge, his calm judgment, and his objective reasoning should furnish him with the rules which will determine the application of these natural laws in practice    It is only thus that the clinician can be clinical in the true sense of the word, a far different matter from the mere calculation of figures or the counting of cells, in giving equal consideration to all the endogenous and exogenous factors that can contribute to modify the normal state of health    We must not forget that the physician above all should keep in mind the welfare of his patient, his constantly changing state, not in the visible signs of his illness but also in his state of mind, which must necessarily be an important factor in the success of the treatment    One would be blind not to recognize that before and even after the advent of modern scientific medicine there were great and able healers of the sick who were not men of science but who had the ability to reassure the patient and thus favourably to influence the course of the illness    It is also obvious that there have been excellent scientists who were very mediocre practitioners    History teaches us that any division of the science and the art of medicine is necessarily harmful to practice "

—ARTURO CASTIGLIONI

—"Do not be like the spider, man, and spin conversation incessantly out of thine own bowels "

—SAMUEL JOHNSON

—"The sins of the colon are its diseases    But I sometimes wonder whether it is not more sinned against than sinning, for what with attacks from above with purges, attacks from below with douches, and frontal attacks by the surgeon, its sorrows are numerous and real "

—"The atonic stomach or colon is often referred to as if it were one in which peristalsis was deficient, but peristalsis is often very active in the presence of hypotonus and may be weak or irregular in the presence of hypertonus "

—"The only movement of importance occurring in the colon is the 'mass peristalsis,' which moves rapidly along a considerable length of the bowel, two or three times a day, carrying all the contents before it    It results from a gastro-colic reflex, which follows the entrance of food into the empty stomach    During the greater part of the day the caecum, ascending colon, and pelvic colon are more or less full, but the rest of the colon is generally empty "

—"It is a surgical aphorism that no operation should be performed on the stomach in the absence of a demonstrable lesion, and I look forward to the time when a similar aphorism will be applied to the colon "

—ARTHUR F. HURST

# The Indian Physician

VOL IV NO 10

OCTOBER 1945

WHOLE NO 46

## Original Contributions

### THE DEFICIENCY FACTOR IN THE AETIOLOGY OF PORTAL CIRRHOSIS IN THE PUNJAB

A PRELIMINARY REPORT

by

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In opening his discussion of cirrhosis of the liver, Rokitansky remarked that "in reference to its pathogeny, "it is one of the most enigmatic affections of the liver" That was in 1846, and it might have been written today The aetiology of portal cirrhosis is still obscure

The opinion that portal cirrhosis (Laennec's cirrhosis or multilobular cirrhosis or atrophic cirrhosis) is caused by the excessive use of alcohol is very deep-rooted and traditionally accepted A critical analysis of the observations made by various workers from time to time, however, does not support this view In fact, there is strong evidence against the direct relationship of alcohol to cirrhosis The earlier pathologists (Orth) had noticed that the typical liver of the drunkard was not cirrhotic but the large fatty type and this has been amply confirmed by subsequent observations (Fahı, Oertel Janeway and others) It has also been observed that in countries where large quantities of alcohol are consumed, cirrhosis is comparatively rare, while it is often very common where the consumption of alcohol is rather small It has further been advanced that alcohol, or in its absence other gastro-intestinal irritants, or vitamin deficiencies (especially of vit A & B) produce a gastro-intestinal catarrh, leading to a changed state of the bowel and affecting its absorptive power and probably resulting in the ingress of certain toxins leading to hepatic deterioration by direct action Some low types of infection (sub-infection of Adamı, 1911) acting on the already depressed liver cells and the connective tissue have also been incriminated Others have blamed dysenteries, spirochaetal infections and various other bacterial toxins Hughes and Shrivastava (1926-1927-1933) were of the opinion that in the Punjab it was connected with malarial infection especially if complicated by severe jaundice They, however, could not establish this on any direct evidence Their study also excluded alcohol

That a hypothetical toxin emanating either from the diseased bowel wall, or from the defective metabolism of the main food constituents, or from bacterial infections of the portal areas, has a deleterious effect on the liver, resulting in this morbid change—is all that can be said at present

Cirrhosis of the liver in animals has been experimentally produced by abnormal diets (Blumberg and McCollum 1941—Chalkoff et al 1943—Gyorgy 1942—Lille et al—1941) Himsworth and Glynn (1944) found that rats kept on a low protein diet developed massive hepatic necrosis According to them carbohydrate, fat, vitamin, mineral and choline content of diet did not exert more than, at most, a modifying influence, the determining factor being the amount of protein eaten daily As they found that casein, even in small amounts, protects against the lesion, while yeast protein even in liberal amounts fails to protect, they concluded that the protective factor was a component of protein rather than an intact protein molecule They tested various amino-acids and found that complete protection was given by methionine They came to the conclusion that dietetic hepatic necrosis (massive necrosis) was a deficiency disease caused by deficiency of a component of protein and prevented by administration of methionine To this they have given the name of "Trophopathic Hepatitis" They also noticed that massive hepatic necrosis thus caused was always followed by scarring and in those animals which survived for any length of time was followed by nodular hyperplasia The picture thus obtained was that of portal cirrhosis from which it becomes indistinguishable at this stage both clinically and microscopically

According to them true portal cirrhosis can also be produced in animals by other dietetic means but in that there is no necrosis (as is the case in trophopathic hepatitis) but fatty infiltration and also uniform fibrosis throughout the organ The resulting end picture in both the cases is similar Consequently—although no conclusive evidence of the occurrence of massive hepatic necrosis due to a deficient diet has yet been produced in man—it is suggestive, that in cases where the recognised causes of portal cirrhosis (like alcohol, etc) are absent, this deficiency factor may be the causative agent Himsworth and Glynn concluded from this that the cirrhosis of liver common in the poor people of Punjab and Rand (Africa) for which no satisfactory explanation had been found, was in fact the final stage of a trophopathic hepatitis due to a dietary deficiency of protein—a condition which, when fully developed, resembles true portal cirrhosis

Gillman (1944) investigating the effect of feeding rats on the diet habitually eaten by the affected natives of Rand (maize meal and sour milk—having a very low protein content) found that the rats developed cirrhosis of liver Other workers have also shown the protective action of methionine Miller and Whipple (1942) demonstrated that in protein-deficient dogs chloroform produced fatal liver damage and this was prevented by giving methionine before it Beattie and others (1944) cured a case of carbon-tetrachloride

poisoning by giving methionine by mouth and methionine and casein digest intravenously. They were of the opinion that the real cause of the liver disturbance induced by carbon-tetrachloride would appear to be abnormal metabolism of sulphur containing amino-acid methionine. Beattie and Marshall (1944) could also protect the liver cells against arsenicals by simultaneous administration of methionine. One is therefore led to conclude that methionine protects the liver against damage from toxic substances. However, the recent therapeutic trials of methionine (Wilson, Pollock and Harris 1945—Higgins et al—1945) in Infective Hepatitis (Toxicopathic Hepatitis of Hims-worth and Glynn) have proved to be ineffective. It would therefore appear that continued deficiency of methionine, either due to a poor intake on economic grounds, or resulting from deficient absorption consequent upon a diseased state of the bowel with normal intake, leads to hepatic necrosis (Tropho-pathic Hepatitis) finally ending in the accepted picture of cirrhosis.

Our present investigations were started to investigate the probable role of this dietary deficiency factor in the causation of portal cirrhosis as it occurs in the Punjab. The investigations are still in the preliminary stages and the only excuse for this publication is to stimulate the interest of others, for if the mystery of the aetiology of this very common and serious malady could be solved, perhaps more successful measures of its prevention could be exercised.

#### A CASE OF PORTAL CIRRHOSIS WITH RECOVERY —

Ch Lal Din M.M. 54 years admitted into the V J Hospital 9th January 1944. 6 months previously had anorexia, gastric discomfort after meals, debility and weakness and constipation. Had a little rise of temperature treated for malaria—no improvement—2 months later had distension of abdomen after meals and colicky pains. Condition deteriorated. Had sleeplessness and restlessness and inability to do work. Swelling of abdomen—admitted into a District Hospital—treated as cirrhosis liver—tapped and 4 pints of fluid removed—fluid reaccumulated. Admitted into V J Hospital.

##### Condition on admission —

Sallow pinched face, prominent nose, slightly anaemic, no jaundice, extreme asthenia and generalised wasting of subcutaneous fat, slight oedema of the lower extremities and also of sacral region. Complained of bleeding from gums and epistaxis, had furred dirty tongue. Abdomen very much distended and prominent dilated veins on abdominal wall in the epigastric region. Abdomen had free fluid. Liver not palpable but spleen one finger below costal margin. Other systems—no abnormality.

Clinical Diagnosis:—Portal cirrhosis (ascites).

##### Laboratory Examinations —

Blood —Hb=90%—Total R.B.C.=4200000/ Cmm. Total W.B.C.=8,000/ Cmm.  
—D.L.C=Polys=53% Lymphos=45% Large Monos=1% Eosins=1%

I an-den Bergh Reaction:—Both direct and indirect negative. Icteric Index=3.

Urine —Sp gr 1032, Urobilinogen+ —

Stools —Normal

Fractional Gastric Analysis —No abnormality.

Ascitic Fluid —Transudate, yellow, clear, no clot on standing, sp gr 1010—Alkaline reaction—Albumin=1.5%, —Microscopic Examination—Occasional Leucocytes and red cells.

Treatment —Saline diuretics and purgatives. Neo Hepatex intra muscularly, 4 c.c. every fourth day.

Diet —High protein—low fat diet. The preponderating proteins were those of milk in the form of skimmed milk, cheese and dahl and also eggs and lean boiled mutton.

Blood Transfusion —Was given twice—450 c.c. from a normal healthy person on the 7th of February and again 400 c.c. on the 26th of February.

Progress —Tapped on 14th January and about 10 pints of fluid removed and 2 c.c. Neptal injected intraperitoneally. Fluid reaccumulated shortly afterwards. Tapped again on 11th of February and about 6 pints of fluid removed and 4 c.c. Neptal injected intraperitoneally. The fluid did reaccumulate but much less in quantity. Tapped again on the 6th of March and about 4 pints of fluid removed and Neptal given intraperitoneally. No fluid reaccumulation after this. All other symptoms had also been progressively diminishing. After the third tap—did not have any complaints—kept on the high protein diet for 3 weeks—discharged from the hospital on the 27th of March with instructions to keep on the high protein diet. Fit and working now.

(Note —No liver function tests were done on this patient.)

Although it was obvious from this case that the improvement was mainly due to the high protein diet and blood transfusions—the rationale of this became more clear, as a result of the work of Hims-worth and Glynn (1944) on rats. The beneficial effects of blood transfusion could also be interpreted to be due to the presence of amino-acids in it (about 3 to 5 mgms/100 c.c. rising to 6 mgms after meals).

Since the above cited case, all cases of portal cirrhosis admitted to the V J Hospital have been treated on high milk diet (2 srs daily) and carefully observed. Casein digest has now been received from England and it will be possible to give a much more concentrated form of methionine to these patients in future.

For the assessment of the progress made by these cases the "Quick Oral Hippuric Acid Test" is used to gauge the liver function. This test, in addition to being one of the most accurate methods now available of measuring liver function (Quick 1936, Snell and Plunkett 1936, Mateer and McMillan 1943, Probst and Londe 1940, Patel 1943, Raghavan 1943, Boyce and McFetridge 1938, Gordon 1943, Riddell and Anderson 1944), is the most generally applicable, on account of its being safe, inexpensive, simple and not requiring repeated venipuncture (Boyce).

The results of this study are given in a table on page 217.

Eleven cases of advanced portal cirrhosis were put on milk diet and studied. All of them belonged to poor walks of life and thus could not afford diet rich in proteins especially milk proteins. This was confirmed by the patients themselves. In addition they were given symptomatic treatment as diuretics, purgatives, and tapping when necessary. Case No. 6 also had one blood transfusion (500 c.c.) while it was not possible in other cases due to lack of donors.

Case Nos. 1 and 11 did not show any improvement and ultimately died. Their initial results with Hippuric Acid test were very low and judged clinically also they were pretty bad. All the rest 9 cases have definitely improved their liver function on this line of treatment as judged by the Hippuric Acid Test. All these (except No. 3) had in the beginning a low liver function, which gradually improved towards normal, although it did not reach the normal limits except in Case No. 6. The initial liver function of No. 3 was within normal limits—although he had marked clinical signs and symptoms of liver damage. This might be explained on the basis of marked reserve power of the liver as regards its functions though Quick suggests that the reserve power of the liver as regards the hippuric acid synthesis by Glycine production is limited. On treatment—this case responded materially with disappearance of ascites and other clinical symptoms and also increased function of the liver. The other case whose function returned to the lower limits of the normal and whose clinical condition improved dramatically was Case No. 6. It is interesting to note that he had in addition one blood transfusion and the maximum improvement started about a week after that.

The improvement shown by the rest of the cases was not so marked both as regards the liver function test and the clinical condi-

TABLE

Case No	Name	Occupation	Diagnosis	Van den-Berg's Reaction.	Ictero Index	Urine Urobilinogen (Dilution of the urine upto which it is +)	Hippuric Acid Test on Admission { Normal range = 2.5 gm to 3.3 gm }	Hippuric Acid Test after treatment with milk (3 seers daily) & other routine treatment including tapping	Clinical improvement of the patient after treatment.
1	Jan Mohammad	Village Shopkeeper	Portal Cirrhosis with Ascites	Negative	0	1 in 40	0.02 gms	0.56 gms	Died
2	Bakhashesh Singh	Land Tiller	do	do	4	1 in 80	1.61 gms	1.93 gms.	Ascites still there but less than before. Other symptoms also slightly improved
3	Jaggo	Beggar	do	Indirect +	8	1 in 80	2.66 gms	3.07 gms	Ascites disappeared. Other symptoms also relieved
4	Abdul Rahman	Barber	do	Negative	3	1 in 30	1.37 gms	1.98 gms	Left early against advice. Not much apparent clinical improvement.
5	Abdul Rahim	Agriculturist	do had ch malaria before it	Negative	5	1 in 40	1.73 gms	2.1 gms	Only very slight fluid in the flanks remained. General condition much better
6	Mohan Dass	Beggar	Portal Cirrhosis with Ascites	do	6	1 in 80	1.62 gms	2.5 gms also had one Blood transfusion	Ascites disappeared. Discharged perfectly relieved of all symptoms. Maximum improvement after transfusion.
7	Sant Ram	Shopkeeper	do had ch malaria before this.	Indirect +	0	1 in 40	1.55 gms	2.03 gms	Left early against advice. Ascitic fluid less than before
8	Mohul Nalik	Nil	Portal Cirrhosis with Ascites	Negative.	3	1 in 30	1.14 gms	1.68 gms	Ascites still there. Not much apparent improvement clinically
9	Kasim	Land Tiller	do	do	3	1 in 60	1.11 gms	1.8 gms	Ascites still there but less than before
10	Labhu	Shepherd	do	do	4	1 in 80	1.10 gms	1.5 gms	Left early against advice. Ascites somewhat less.
11	Arjan Singh	Land Tiller	do	do	3	1 in 20	0.45 gms		Died

Note.—Disappearance of Ascites or lessened ascites means no reaccumulation or lessened reaccumulation after tapping

tion This was in conformity with what was expected Portal cirrhosis is a gradually progressing disease in which the destroyed liver parenchyma is being gradually replaced by the fibrous tissue hyperplasia with some regeneration of liver cells . So at any stage of the disease, we are dealing with normally functioning liver cells, diseased liver cells and fibrous tissue Methionine exhibited in adequate amounts could only preserve the residual normal liver tissue and prevent further damage of the affected cells but could have no action on the fibrous tissue

#### CONCLUSIONS

This study would seem to suggest the important role of deficiency of protein in diet in the aetiology of portal cirrhosis It thus opens a new era in the prophylaxis and treatment of portal cirrhosis We may not be able to cure such cases on these lines, but their condition can be definitely relieved It is obvious that if their treatment is started sufficiently early, when much fibrous tissue has not been formed—they may be benefited greatly It has to be realised that the clinical text book picture of cirrhosis, as taught to the medical students, is the termination of a slowly progressive affection of the liver extending over a number of years, very often not recognised unless looked for If, however, a direct relationship could be established between the deficiency factor and this morbid process, it would appear that much can be done to prevent an almost fatal disease when fully developed With the evolution of delicate—although yet evasive—hepatic function tests, it should not be difficult to detect the early incidence of the disease and apply the appropriate remedy Even the beneficial effects of amino-acid substitution therapy would obviously depend upon the residual hepatic parenchyma available for regeneration and therefore this measure is not likely to succeed when none is available Thus portal cirrhosis would appear to be a preventable disease and offers itself for preventive attack over a number of years

The investigations are being continued on the above lines with casein digest instead of milk

We are grateful to Professor J Beattie, Bernhard Baron Research Professor of Royal College of Surgeons England and the British Colloids Ltd., Bombay (Mr Ernest Proc Manager) for the supply of casein digest free of cost.

We also express our thanks to the Inspector General of Civil Hospitals Punjab for the funds placed at our disposal and the Medical Superintendent and the staff of V J Hospital Amritsar for their help and co-operation.

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# PRIMARY PERITONITIS IN CHILDREN\*

by

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Primary peritonitis is a condition which is comparatively common in childhood, it is still associated with a forbidding mortality and there is still no unanimity of opinion about its treatment. It is possible that penicillin might furnish a clue to the ultimate treatment of the disease. Only one of the cases reported in this series, however, was treated by penicillin and that case survived. The remainder had the misfortune to come for treatment, before penicillin was freely available for civilian use.

Of the 8 cases reported in this series, only four are personal cases. The remainder have been treated by other members of the staff at the Children's Hospital, but I have been fortunate enough to follow all but one of these cases through, from the beginning to the end of their illness. These cases represent only those cases of primary peritonitis that have come to the Jerbai Wadia Hospital and the K.E.M. Hospital in the last three years.

Primary peritonitis is defined as a peritonitis in which there is no demonstrable focus of infection in the abdomen or in the rest of the body, strictly speaking, there can be no such condition, because pneumococci and streptococci are not normal inhabitants of the peritoneal cavity. There have been 6 cases of primary peritonitis in the Children's Hospital in 3 years, out of a total of 52 cases of acute abdominal conditions, so that, primary peritonitis has constituted roughly 12 per cent of the abdominal emergencies of childhood. The other acute abdominal conditions encountered have been appendicitis, intussusception, pyelitis, round worm obstruction, etc.

The following figures from other clinics (giving the proportion of primary peritonitis to other abdominal emergencies in childhood) show, in the first two series a rough correspondence with the present figures.

Lipshutz and Lowenburg (America) (1)	10%
Great Ormond Street (London) (2)	77%

In the present series of abdominal emergencies, there were 17 cases of acute appendicitis so that the proportion of cases of acute appendicitis to peritonitis is 17/6 or roughly 3/1. These figures are identical with those of Candolin in Finland (2).

All the pneumococcal cases in the present series were females. Of the remaining cases only one was a male. According to Ladd and Gross (3), however, there is only a slight preponderance of females over males, in any large series of cases.

The average age of the sufferers was five years—the youngest child, a case of gonococcal peritonitis—being one month old. All the patients with the exception of one pneumococcal case belonged to

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\* A paper read before the 50th Meeting of the Staff Society of Seth G. S. Medical College Bombay, with Dr. T. O. Shah, F.R.C.S. (Eng.) in the Chair.



the poorer classes. A definite history of diarrhoea which has for so long been considered a symptom of primary diagnostic importance was obtained in only one case and that case had localised to form an abscess at the umbilicus.

Constipation, however, was a pronounced feature in every case at the time of admission to Hospital. An interesting feature of both the pneumococcal and the streptococcal cases was the extreme suddenness of the onset, a previously healthy child, being struck down—without any premonitory symptoms. Frazer (4) has described how in a typical acute case, the mother of the sick child can often fix the exact hour when the illness began.

Clinically there was no evidence of vulvo-vaginitis in any of these cases and therefore it was not thought worthwhile doing a microscopic examination of a vulvo-vaginal smear. Only one of the operated cases showed congestion of the fallopian tubes.

I have personally not attempted diagnostic aspiration of the peritoneum, though it is a method that has been strongly recommended by Lipshutz and Lowenburg (1) and more recently by Leopold and Kaufmann (5). My reasons for not adopting peritoneal puncture as a routine diagnostic measure is the risk that the procedure carries, of injury to the bowel, further, as I have adopted routine exploration in all suspected cases, I thought the procedure unnecessary in addition to being dangerous. However, my colleague at the Jerbai Wadia Hospital, Dr R. V. Sanzgiri has been more venturesome, having done a peritoneal tap on four cases. In two of these, a mixed bacterial flora was found on microscopical examination of the aspirated fluid, suggesting a perforative peritonitis, a diagnosis that was confirmed at the subsequent exploration. In the other two cases, the results were inconclusive. In one case, no peritoneal fluid was sucked up by the syringe, in the other, the microscopical examination of the aspirated fluid revealed no organisms.

I shall epitomize briefly the salient features of the 8 cases which form the basis of this paper.

**PNEUMOCOCCAL PERITONITIS—5 CASES—**4 cases proved by microscopic examination of peritoneal fluid.

(1) Female child 4½ years appendicectomy done after suction of all peritoneal exudate, no drainage. Died 24 hours after operation. Penicillin was obtained and administered just before death. 30 000 units were injected intramuscularly.

(2) Female child—5 years, appendicectomy done after peritoneal suction. Drainage employed, died 6 days after operation of a terminal pneumococcal meningitis and pneumonia, showing the readiness with which any localised pneumococcal infection tends to generalisation through the blood stream. No penicillin was used. An interesting feature of this case was that whereas streptococci were reported from the peritoneal fluid, pneumococci were found in the C S F. This finding bears out the well recognised difficulty of distinguishing morphologically between some strains of pneumococci and streptococci. This difficulty can only be resolved by resorting to cultural methods of differentiation which were unfortunately not employed in this case.

(3) Female child—3 years—simple drainage after peritoneal suction. died 12 hours after the operation. This was the only case with congestion of the fallopian tubes.

(4) Female child—8 years, was admitted with a 15 days' history of diarrhoea and vomiting. There was a localised abscess at the umbilicus. She recovered with incision, evacuation and drainage of the abscess.

(5) Female child—5 years. the diagnosis was not microscopically proved, but this case presented all the clinical signs and symptoms of primary peritonitis. There was a sudden onset of severe abdominal pain with high pyrexia and vomiting—there was no history of diarrhoea and no evidence of a pulmonary lesion. There was profound abdominal rigidity.

This case responded so promptly to two injections of injectable sulfapyridine and to the oral administration of sulapyridine, that the clinical findings and the therapeutic response taken, together lead me to think that this was a case of primary peritonitis probably of pneumococcal origin. The symptoms abated within 24 hours of commencement of the treatment.

## STREPTOCOCCAL PERITONITIS—2 CASES :

(1) Male child—7 years—appendicectomy and drainage done. The only case where penicillin was given a full trial albeit late in the course of the disease (350 000 units). There were two wound breakdowns and finally repair of the abdominal wall with wire sutures ended in healing.

(2) Female child—9 years—a case of typhoid fever that developed all the signs of perforation. At exploration, gas hissed out of and there was turbid fluid in, the peritoneal cavity. Streptococci were found on microscopic examination of the fluid. A thorough exploration revealed no perforation in the gastro-intestinal tract. Bacterial leakage through a thinned devitalised portion of the gut probably accounted for the condition. This child died twenty four hours after operation.

## GONOCOCCAL PERITONITIS—1 CASE

Female child—1 month admitted with a hypogastric lump and a history of retention of urine. There was an umbilical discharge. In view of some doubt as to the nature of the swelling a diagnostic aspiration was done after catheterisation of the bladder had drawn a small quantity of urine. Frank pus was withdrawn. Microscopic examination of the pus showed gonococci. This child, a wasted marasmic infant died a few hours after aspiration.

The problems that arise in connection with treatment of the condition are firstly, whether to operate or not to operate, if the former decision is made the next question that arises is, whether to operate early or late.

With regard to the first question, the dice are heavily weighted in favour of operation. There is no doubt that some cases will localise to an umbilical abscess, with or without treatment. But that would mean the survival of the fittest. Three valid reasons for operating have been adduced by Ladd and Gross (2).

(1) Microscopic examination of the fluid in a case of primary peritonitis, would show whether the infection is pneumococcal or streptococcal. Appropriate chemo-therapeutic measures can then be adopted against the offending organisms.

(2) Cases of secondary perforative peritonitis are not likely to be missed, and appropriate surgical measures can be adopted by way of treatment.

(3) Drainage of the peritoneal fluid by a tube in the pouch of Douglas is a valuable measure in relieving toxæmia.

The second question is answered in favour of early operation. Late operation, in this context, implies waiting for localisation to occur.

By early operation, I do not imply that a shocked moribund child should be explored forthwith. Enough time must be spent in preparing the child for operation. Dehydration must be combated by the administration of adequate amounts of fluid parenterally, distension by a continuous Warngensteen suction and toxæmia by chemotherapy and fluid administration.

The question of a diagnostic peritoneal tap as against the limited peritoneal opening through a small paramedian incision as practised by Salzberg in Vienna and championed by Ladd in America must be resolved in favour of the latter. Microscopic examination of the peritoneal fluid by a small para-umbilical, paramedian incision without exploration would be a safer procedure than a blind peritoneal puncture.

In view of the readiness with which penicillin is now available and in the light of experience gained in these cases, I propose in the future, to adopt the following line of action.

(1) Administer penicillin by the intramuscular and/or intra venous route in the waiting period between admission and operation. The object of the initial chemo-therapy being to combat the co-existing septicaemia. Simultaneously, dehydration, distension and toxæmia to be combated. Operating upon a primary peritonitis in the presence of a fulminating pneumococcal septicaemia might be compared to operating upon an empyema in the presence of a raging pneumonia.

(2) When the child has rallied sufficiently, explore the peritoneal cavity through a small paramedian incision at the level of the umbilicus, and remove some of the contained pus for microscopy and culture. I would make sure the microscopist was present in the operating theatre with a microscope, so that I could get an immediate report, much the same technique as is adopted in frozen section reports in exploration for suspected malignancy. While the microscopy is proceeding, cover the wound with a sterile towel.

If the examination reveals pure pneumococcal or streptococcal infection, insert a rubber drain into the pouch of Douglas and proceed to a closure. Minimum retraction and trauma should be the watchword.

No appendicectomy should be done, as it might turn the scales against a gravely ill patient. After the operation, penicillin should be continued intramuscularly and into the peritoneal cavity through the drainage tube. I do not claim any originality for this line of treatment. The method was adopted by Salzberg in the pre-penicillin and pre-sulphonamide era in Vienna. Needless to say, the advent of the sulphonamides has made a big difference to the mortality figures of this grave disease. It is to be hoped that penicillin will furnish the final answer.

The following mortality figures quoted from Ladd and Gross(2) might be of interest. From the present series, no conclusions as to percentages has been drawn, as the number of cases treated has been too small.

MORTALITY RATES IN PNEUMOCOCCAL AND STREPTOCOCCAL PERITONITIS

Author	Year Reported.	Pneumococcal Peritonitis	Streptococcal Peritonitis
Lipshutz and Lowenburg	1926	100%	100%
Ladd	1930	66%	65%
Donovan	1934	75%	78%
Leopold and Kaufmann	1937	Nil	91%
Ladd & Gross	1940	12%	22%
Present Series	1944-45	(5 Cases—2 Survived) Of the surviving cases one not microscopical ly proved	2 Cases. 1 Survived

The figures of Ladd and Gross in 1940 are striking evidence of the efficacy of the line of treatment they have followed.

In conclusion Dr DeSa thanked Dr Cooper for having consented to his using the clinical material of the Jerbai Wadia Hospital and Dr R V Sanzgiri for helpful suggestions and advice. He also thanked Dr Dastur, Surgical Registrar of the Jerbai Wadia Hospital for valuable assistance and co-operation.

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## DISCUSSION

Dr V P Mehta said "Primary peritonitis has been an extremely fatal condition and in the literature we find authorities like Barrington-Ward, Bruce and Logie, Moreton, Rischbieth give an almost 100 per cent mortality

Charles Noon has been interested in this subject for more than ten years and has been successful in reporting four consecutive cases without a single death. Three of these cases were treated by laparotomy, drainage and Felton's serum and all of them recovered after a stormy and long convalescence lasting about eight to ten weeks. The fourth case was treated by laparotomy, drainage and sulphapyridine, and the patient caused no anxiety during convalescence which lasted only five weeks. Arnold (1940) claims to have saved a severe case due to pneumococcus type V, by immuno-transfusion. He gave to a suitable donor an injection of 100 million typhoid organisms and seven hours later the temperature rose to 104°F and the total WBC count was 40,000. 300 cc of blood were taken from the donor and transferred into the patient. There was a dramatic response in 24 hours when the pulse and temperature improved. Two more transfusions were given after 48 hours. Later a localised intraperitoneal abscess was drained. An empyema was opened and drained. Recovery was complete. Paracentesis abdominis has been suggested as a diagnostic measure and Loewe has suggested puncture through the posterior vaginal fornix as the puncture is more likely to be helpful.

Dr R. G. Dhayagude said that Dr DeSa had referred to a case in which the peritoneal exudate showed organisms of the nature of enterococci and which later examination proved to be pneumococci. The differentiation between the streptococcus and pneumococcus, especially in cultures, was known to be difficult and various methods are employed in their identification. He then referred to the series presented by Dr DeSa and pointed out that the diagnosis of the smear examination was confirmed by cultural examination in only one case. He suggested that blood cultures should be done in every case as he felt that septicaemia was either a primary or secondary event in a large proportion of cases of peritonitis. In those cases in which septicaemia was primary he doubted whether surgery has any place in the treatment. At any rate he recommended that in those cases chemotherapeutic agents must be given a trial before resorting to the knife.

Dr C B Dhurandhar suggested the intraperitoneal use of penicillin as in his experience local instillation of penicillin in the eye in cases of gonococcal affections such as conjunctivitis, ulcers of the cornea and chronic dacryocystitis yielded good results, the causative organisms disappearing in 24 hours.

Replying to the various questions raised, Dr DeSa said that there were technical difficulties in the way of diagnostic vaginal aspiration, in such small children, but the method of peritoneal drainage by posterior colpotomy had been advocated by McCartney and Frazer (6) as far back as 1921

The reason why serum had not been used in the treatment of the pneumococcal cases was that a type-specific serum had to be used, and there are over thirty strains of pneumococci. There were difficulties in obtaining an immediate typing of the organism, and there were difficulties in the way of obtaining the serum, apart from the expense of the treatment in charity patients. He agreed with Prof Dhayagude that if culture of the peritoneal fluid had been made in Case (2) of the pneumococcal series—there should probably have been no discrepancy in the peritoneal and C.S.F. findings

Dr T O Shah in his concluding remarks said that in this important subject with a high mortality, a close study was necessary. Gonococcal peritonitis arose secondarily to a lesion in the Fallopian tubes. As regards the value of exploratory puncture, he was of the opinion that it was of little value and that the risk of injuring the intestine was considerable. Exploration should be resorted to only when there was a localised collection of pus. He emphasized the need for cultural study of the organisms from these cases. In the treatment he mentioned penicillin as an effective weapon.

# A NOTE ON LOBECTOMY

by

M. M. PANDYA, F.R.C.S. (Eng.)

K. E. M. Hospital, Bombay

Dr M M Pandya reported two cases of lobectomy both with fatal results. These were the only two cases to be operated in the K.E.M. Hospital from the time of its inception. He reviewed the progress in the cure of the diseases of the chest with especial reference to the application of surgical principles in a field which hitherto was considered to be a physician's realm.

## Case Reports.

**Case 1**—Male, 7 years, admitted in medical wards in August 1938 for cough and foul expectoration for three years. No history of hemoptysis or tuberculosis. Examination of the chest showed deficient air entries second and third intercostal space right side and rales at the bases. There was no clapping. The quantity of sputum was two or three ounces per 24 hours. Skiagram showed a lung abscess right upper lobe. Medical treatment for six months including bronchoscopic aspiration was fruitless. The patient was operated in April 1939.

*Details of operation*—The patient was operated under open C E general anaesthesia by an intercostal incision in the 4th intercostal space. Parietal as well as interlobar adhesions were cut and the lobe isolated and removed between two tourniquets. Vascular and bronchial stump was closed by continuous suture. This was covered over by a continuous suture in the lung tissue. Thorax was closed with drainage. Immediately on removal of the patient from the operating table to the trolley the patient became cyanosed and respiration stopped and the patient died. The cause of death very probably was due to the squeezed out secretion from the operated side entering the bronchus of the only functioning lung. This could have been avoided by intra-tracheal anaesthesia and suction of the collected discharge at the end of the operation.

**Case 2**—Male, 52 years, admitted for pain in the right side of the chest. Foul breath and fever for six months. History of pneumonia eight months ago. Examination of respiratory system revealed diminished movements in the right side, a dull percussion note right infra-axillary region and rales at the bases. There was marked clubbing of the fingers and quantity of sputum expectorated in 24 hours was 4 to 6 ounces. Radiological examination showed a cavity with fibrosis in the right lower lobe. Sputum elastic fibres but no M tuberculosis.

The pre-operative treatment consisted in absolute rest for two weeks, postural drainage and three blood transfusions. The operation was done under intra-tracheal cyclopropane.

*Details of operation*—Major thorotomy through the sixth intercostal space. Lobe was markedly adherent. The adhesions were cut and the lobe isolated and removed in the same way as in the first case. The thorax was closed with drainage.

Immediately after the operation the blood pressure fell to 95 mm Hg systolic but after 24 hours the blood pressure improved. The lung was completely expanded, the same evening the patient complained of a sudden pain in the chest, dyspnoea and there was a rapid pulse and spreading emphysema. The wounds were re-opened next day but there was no haemorrhage in the pleural cavity and no pneumothorax. The line of suture in the lungs had almost healed and could be identified with difficulty. There was temporary improvement but the patient expired the next morning four days after the operation. The probable cause of death in this case was pulmonary embolism.

Dr Pandya made then a few observations, mentioning that his series included only two cases, a small number to draw any definite conclusions. A scheme in the treatment of this type of case was outlined as follows —

- 1 A pre-operative blood transfusion and special unit for work.
- 2 Intratracheal cyclopropane was the ideal anaesthetic
- 3 A preliminary A. P. was not necessary. A small opening in the parietal pleura with a regulating pressure of a finger allowed a slow collapse of the lung and prevented mediastinal flutter
- 4 Pleural adhesions can be easily separated without diathermy
- 5 It is not necessary to separate the diseased lobe to the root of the lung. The only hindrance to the operation was the diaphragmatic movement which could be stopped by infiltrating the phrenic nerve with novocain or by crushing, the consequent delay in the expansion of the remaining lung is more than compensated by the ease of operation, and local post-operative rest

In concluding he made a plea for a more rational line of treatment in lung abscesses. A preliminary period of medical treatment with postural and bronchoscopic aspiration should be given a trial, but not persisted with if improvement is not seen. If six weeks after the bronchial drainage has been established the condition does not improve, then further surgical intervention is necessary. Delay brings in its train further complications like secondary bronchiectasis which precludes successful open drainage. A certain number of other cases are either not recognised or presented for treatment late when fibrosis and epithelialization of the cavity has occurred. The only treatment in these cases is lobectomy. A similar line of treatment is justified for unilobar bronchiectasis.

# Case Report

## "THE COMMON COLD" AND "BAD THROAT"

### AND THEIR SEQUELAE SOME IMPORTANT CONSIDERATIONS IN TREATMENT

by

S K VAIDYA, L.M. & S (Bom.), M R C S (Eng)  
D.P.H (Cantab) D T.M II (Cantab)  
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It is not often that practitioners of the Art of Medicine get either an opportunity of observing critically such an ever-present usually-transient complaint as "the common cold" slowly developing its more disabling complications such as tracheitis and nasal sinusitis, or of carefully noting down the subjective symptoms and the response to the day-to-day hesitating, changing treatment. And yet in the aggregate, it is one of the most frequent semi-disabling maladies, a proper appreciation and right treatment of which would be most welcome to practically the whole of humanity.

Having had two such opportunities recently within the last six weeks, the present writer deems it essential to place his experience before the medical profession with a view to adding ever so little to the already accumulated fund of recorded knowledge on the subject and will consider his effort well-rewarded if it helps even to some small extent the average medical practitioner to add to his knowledge in fighting this scourge of humanity.

**The Case** —S Male, Indian. Age 64 years lean of build weight 95 lbs. generally of fairly good steady eventless health, of abstemious habits a strict vegetarian living mostly on weak tea four times a day with about three ounces of milk each time, about half an ounce of Indian whole unsplit pulse grains, such as *Moong* (green gram) *Val* (field bean) *Chana* (Bengal gram), *Urd* (Black gram) mostly germinated and cooked in salt water, and four to five *Tolas* (about two ounces) of whole wheat meal *Dhalia* or porridge with milk and two small *Elachi kelas* (plantains golden) per 24 hours with some leaf vegetable once a day rarely falling ill and intermittently taking Arsenic and a little potassium iodide if indicated with a little quinine some times. His Normal range of temperature is 97.6 F in the mouth in the early morning to 98.6 F in the evening and pulse rate is normally sixty or sixty two per minute, while his normal blood picture is 60-70 per cent neutrophils and 2-4 per cent eosinophils with total leucocytes about 5-6000 per cmm and both RBC and Hb are between 95 per cent and 100 per cent.

The first time the illness commenced on 18.7.45 with naso-pharyngeal trouble which was described as 'Bad throat, with hoarse voice with pain and a little sputum (mainly throat secretion) and temp 99°F in the evenings with a feeling of 'warmth' or feverishness since two days previously. As the weakness and feeling of fatigue increased the following treatment was started.

Date.	Time.	Treatment	Remarks
18.7.45	2 p.m.	4 tablets Sulphathiazole 0.5 Gm each (=2 grams)	1 everish feeling poor sleep no nasal 'cold'
"	6 p.m.	2 Tablets do (1 Gm)	No nasal 'cold'
"	11 p.m.	2 Tablets do (1 Gm)	Temp 99.6°F
19.7.45	7 a.m.	1 Tablet do (5 Gm)	Temp 98.4°F Pulse 60-70 p.m
"	1 p.m.	1 Tablet do (5 Gm)	Temp 99.0°F
"	7 p.m.	2 Tablets do (1 Gm)	Temp 99.8° 100°F
20.7.45	0-80 a.m.	Temp was 100°F while Pulserate was 72 p.m	
Blood Leucocyte counts were done			
Total leucocyte-count —3800 per cmm —Leucopenia			
Differential—leucocyte count (100) as under —			
	Polymorph neutrophils	63%	
	Eosinophils	7% increase	
	Basophils (mastcells)	1%	
	Hyalines (monocytes)	8%	
	Lymphocytes	21%	

100



*N.B.*—There was no inflammatory type neutrophil leucocytosis while there was *relative eosinophilia*. It was therefore decided to stop sulphathiazole treatment, and to give Arsenic and quinine

20-7-45	8 a.m.	3 grs Qn DiHCl2	Temp 99.6°F
"	2 p.m.	3 grs Qn DiHCl2	Temp 100°F Took 1 mango & 2 small boiled potatoes
"	7-30 p.m.	3 grs Qn DiHCl2	Temp 100°F
21 7-45	5-30 a.m.	3 grs Qn DiHCl2	Temp 98°F
"	7-30 p.m.	3 grs Qn DiHCl2	Temp 98.6°F
22 7-45	7 a.m.	3 grs Qn DiHCl2	Temp 97.8°F
"	7-30 p.m.	No Qn DiHCl2	Sputum and Tracheitis started
"			Temp 98.6°F
23 7-45	6-45 a.m.	3 grs Qn DiHCl2	Temp 97.2°F Tracheitis sputum Glottis irritation
"	7 30 p.m.	No Qn	Feeling 'warm' Temp 98.2°F
24 7-45	6-30 a.m.	3 grs Qn DiHCl2	Temp 97.2°F
		10 minims Arsen Hg I	Tracheitis contd
		5 grs KI	
25th & onwards	Daily	do once a day	Tracheitis contd for a week more.

This attack travelled down the trachea and continued fairly long with only low temp much sputum and practically no nasal trouble

The second attack of COLD commenced only a week ago on Sunday 26th August 1945, with sneezing low temperature—99°F a 'funny throat', and the Pt. felt bad also on Monday and Tuesday and was treated with 6 grs. of Quinine DiHydrochloride per day. The condition did not appear to come under control and by Tuesday evening the Temp was 100.2°F with marked feeling of 'warmth' (feverishness) and a stuffy nose. So a change in the line of treatment was felt necessary —

Date.	Time.	Treatment.	Remarks
28 8-45	7 p.m.	3 tablets sulphathiazole 0.5 Gm each	Temp 100.2°F nose stuffy
"	11 p.m.	2 more tablets of S-Thiaz	Temp 101.8°F with 2-3 bouts of mild 'chill' (rigor)
29 8-45	6 a.m.	No medicine during the whole day and night.	T 101°F Felt very bad nausea
30 8-45	6 a.m.	No medicines during day	T 101.4°F felt bad
		Took 12 grs QnDiHCl2 during night, 3 grs every 8 hours	T 99.4°F morning rose to 100° in afternoon
31 8-45	6 a.m.	Again hesitation in line of treatment	No nausea nose blocked felt bad T 100°F Only fruit juice for 2 days No tea even
"	8 a.m.	Changed to S-thiazole 2 tablets (1Gm) with tea.	T 99.6°F felt bad nose stuffy and burning
"		But doubt remained about correctness of line of treatment So	
"	at 10 30 a.m	Blood leucocyte-counts were done	
		Total leucocytes count —6200 per cmm.	
		Differential—leuco-count (200) as under —	
		Polymorph neutrophils	74%
		Eosinophils	0.5%
		Basophils (mastcells)	0%
		Hyalines (monocytes)	9%
		Lymphocytes	10.5%

100 0

*N.B.*—There was a definite decrease of eosinophils and lymphocytes with neutrophil increase

So it was decided to continue S-Thiazole treatment. But only 1 tablet of 0.5 Gm each every six hours with a view to avoid producing toxic nausea, etc.

ctd 31 8-45	2 p.m.	1 S-thiaz tab 0.5 Gm no sweet fruit juice Took salty-cholai leaf vegetable soup and 1 tola and Moong (about ½ an ounce) and 1 lemon juice	T 100.2°F at 3 p.m. 101°F at 6 p.m. 101.4°F at 7-30 p.m.
31 8-45	8 p.m.	1 S Thiaz tab 0.5 Gm	Temp 100.8°F at 10 p.m.
1 9-45	0 30 a.m.	1 S Thiaz. tab with tea	T 100°F
"	6 a.m.	1 S-Thiaz tab 0.5 Gm with tea	T 99.4°F feeling better, nose clearer
"	12 noon	1 tab S-thiazole 0.5 Gm with Moong water soup with salt and lemon juice	T 98.6°F
"	6 p.m.	1 tab again of S Thiaz	T 99.4°F
"	7 p.m.	took Cholai Bhajec-leaf and water with salt and lemon juice.	T 99.4°F at 8 p.m.
2 9-45	0 Midnight	1 tab S thiaz. 0.5 Gm with tea	woke up with sweating T 98°F felt well and nose clear
	6-30 a.m.	1 tab S thiaz. 0.5 Gm with tea.	T 97.8°F

*It was now decided to stop a Thiazole treatment and not to restart unless the temp again began to rise and nasal stuffiness returned*

2-9-45	12 noon	No treatment, took tea.	T 98°F
	6 p.m.	No treatment, Cholai bhajee	T 98.4°F
3-9-45	0 Midnight	No treatment, took tea.	T 98.2°F well
	5 a.m.	No treatment, took tea	T 97.8°F well

It will be noted that while both the times the illness started with an attack of "cold" either in the throat or the head (nose), the further progress of the two conditions and the response to treatment in each case was quite different. The blood examination in the first condition reveals an increase in eosinophils with leucopenia (unfortunately this was noted *only after* 12 tablets (6 gms) of sulphathiazole and it cannot be said with confidence whether the leucopenia was due to the infecting agent or due to the chemotherapeutic treatment) and inferring therefrom, and I believe rightly, that the causative agent was an allergen, s-thiazole treatment was stopped and QnHCl<sub>2</sub>, and in the end Arsenic and KI, were adopted. The involvement of the trachea with sputum also supports this view. It has been invariably observed by the writer that whenever a case of "the common cold" is associated with eosinophilic blood-change, it responds best to arsenicals in some form supplemented by KI and if necessary because of the slight feeling of 'feverishness' with 2-3 grs of quinine, per day, either the bisulphate or the dihydrochloride, and

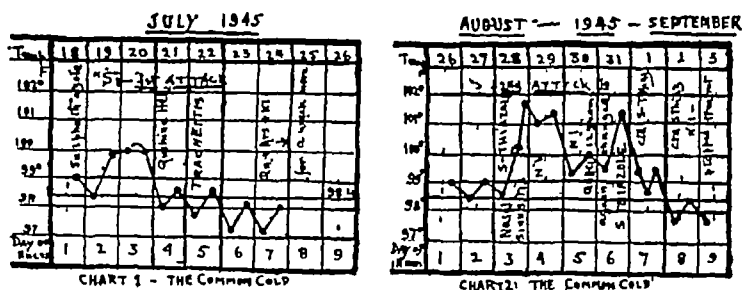


Fig Showing temperature charts of two attacks of 'common cold'

after about a week or so the purulent sputum which at first is sticky and difficult to bring up begins getting less and less and the tracheitis clears up leaving practically no reminder of the condition behind. On the other hand if there is no eosinophilic response, but *even a decrease* of these cells from their normal level, the condition does not respond easily to arsenical-cum KI treatment, as was found to be the case in the second illness in this patient. One other peculiarity also marks it out as quite another illness when we pay proper attention to the further spread of the infection. While in the first condition the nasal mucosa and the sinuses were practically left alone, the infection spread to the larynx and the trachea and the temperature rise was not very marked. *But* in the second illness, the infection, instead of spreading downwards as before, involved the nasal mucosa almost from the beginning and by the third day the nasal sinuses were markedly inflamed and blocked with oppressive tender areas over the nasal bridge and below the frontal sinuses and every res-

piration caused a sense of suffocation and burning sensation during expiration

As the previous condition had yielded to the arsenical-cum KI treatment and as the first time eosinophilia was found, it was sub-consciously assumed that the second time also the illness might be the result of the same infecting allergic agent and in spite of the presence of the painful distressing sinusitis, a doubt was created and proper treatment, i.e., anti-inflammatory line of treatment by an appropriate sulphonamide-derivative, could not be carried out with confidence, *until blood examination was done* The moment eosinophils were found to be practically absent, and neutrophils' tendency to rise was noted, all doubt was set at rest and steady treatment with sulphathiazole in moderate doses only for two days, amounting in all to 10 tablets (5 Gms) the second time, practically cured the condition with very marked relief in the subjective feeling and distress only after the first six tablets were given

I consider even the slight lowering of temperature after the first exhibition of S-thiazole —5 tablets during the first night, which was noted on the 30th morning, in spite of giving no treatment during the interval, was due to that first treatment and it was unfortunate that the slight nausea and the doubt in the mind about appropriateness or not of that line of treatment led to hesitation and change, by shifting on to Qn DIHCL<sub>2</sub> treatment, on the assumption that this second illness was also due to the eosinophil response-type allergen

#### CONCLUSION

The moral to be drawn from this experience of the progress in the two attacks of "The Common Cold", their spread in different directions, selecting for attack quite different mucosal areas with distinctive blood-responses, is that though the conditions in the same patient began as "common colds and bad throats," were in fact due to different infecting agents and only yielded to the appropriate lines of treatment quite different in each case, when such lines were laid down intelligently after blood examination and persisted in without doubt and hesitation

Such a scientific approach to diagnosis as to causative agents and their appropriate treatment by the indicated medicinal agents, would make the lot of the practitioners of the Art and Science of Medicine at the same time more satisfying and easy

# Critical Notes & Abstracts

## DILANTIN SODIUM AND FOCAL SYMPTOMATIC EPILEPSY

Although it is recognised that the sensory manifestations of a localized epileptic disturbance may include the element of pain, they are not usually confined to a single somatic segment or focal visceral area. Furthermore, localized pain, as an isolated phenomenon not associated with somatic convulsive seizures or with other motor, sensory, or psychic variants of epilepsy would rarely be considered a form of epilepsy even though its occurrence was episodic and paroxysmal.

M T Moore (J.A.M.A. 124 561, 1944) reports successful treatment with dilantin sodium of a man who had irregular attacks of isolated paroxysmal abdominal pain over a period of twenty-nine years, with treatment based on consideration of such conditions as hysteria, abdominal angioneurotic edema, abdominal migraine, psychogenic functional gastrointestinal disorder, hepatobiliary disease, enlarged colon, Dietl's crisis, and diaphragmatic hernia.

Negative results from previous treatment, the complete absence of any specific etiologic factor, and the periodic pattern of the abdominal pain, suggested a form of focal symptomatic epilepsy, and it was thought advisable to have electroencephalography carried out. The first encephalogram showed abnormal waves, particularly in the right and left frontal lobes. As a result of these findings the patient was started on dilantin sodium 0.1 Gm ( $1\frac{1}{2}$ gr) twice daily and 1 fluid-drachm of a mild bromide mixture four times daily. This therapy brought about a prompt cessation of attacks and a second encephalogram taken approximately six months later showed a restoration of the alpha activity throughout the cortex except under conditions of hyperventilation when delta activity could be seen.

When this report was submitted the patient had been free from attacks for fifteen months during which time he received dilantin sodium 0.1 Gm ( $1\frac{1}{2}$  gr) twice daily. The bromide mixture was taken irregularly during this period.

The explanation offered by Moore, as to the possible etiologic basis for the localized epileptic disturbance, expressed by abdominal pain, is that the cerebral cortex, especially of the frontal lobes, was injured or sensitized by injection of diphtheria antitoxin when the patient was 9 months of age, producing a cerebral angioneurotic edema, the altered brain tissue becoming the seat of abnormal electrical discharges.

## SALICYLATE THERAPY IN RHEUMATIC FEVER

Main objective in treatment of rheumatic fever is reduction of cardiac damage to a minimum by suppression of the rheumatic inflammatory reaction. The only drug in general use for this purpose is salicylate and there is no consensus concerning its value in suppressing the inflammatory reaction of rheumatic fever.

A F Coburn (Bull Johns Hopkins Hosp 73 435, 1943) says that maintenance of a plasma salicylate level of at least 350 gamma per cc tends to suppress the rheumatic reaction in the tissues, whereas maintenance of plasma levels below 200 gamma per cc relieves symptoms but only masks a progressive inflammatory process

Observations on the relation of rheumatic activity to plasma salicylate levels show that 20 patients maintained at 350 to 400 gamma of salicylate per cc manifested a prompt and progressive subsidence of rheumatic inflammation and that 20 other patients with plasma levels below 250 gamma per cc continued to manifest an active inflammatory process

Results of two years' clinical experience with a special technic for giving salicylate show that none of 38 rheumatic patients treated with 10 grams of sodium salicylate daily developed valvular heart disease and that 21 out of 63 similar patients who received only small doses of sodium salicylate developed physical signs of rheumatic carditis

Intravenous administration of sodium salicylate is required to obtain rapid rise in plasma salicylate to 400 gamma per cc or higher. On this basis, Coburn developed a therapeutic scheme of initial use of intravenous and then oral salicylate for rapid development and maintenance of adequate plasma salicylate levels

Ten to 20 gms of sodium salicylate are given intravenously every day for one to three days depending upon fever and other symptoms. Usually on the third to the seventh day, oral medication replaces intravenous treatment and is continued through the thirtieth day of the salicylate regimen. Doses of 16 Gm sodium bicarbonate are given by mouth every four hours day and night

The question of continuation of sodium salicylate administration beyond the thirty day course is determined by the sedimentation rate and by the absence or recurrence of symptoms after the patient is allowed up

The maintenance of a high plasma salicylate concentration represents a valuable method of suppressing the rheumatic process

## **SALICYLATES AND BICARBONATE**

(Small Katherine Wegrin Rene and Leland Jessen. The effect of Sodium Bicarbonate on the Serum Salicylate Level during Salicylate Therapy of Patients with Acute Rheumatic Fever J. L. M. A 725 1173, 1944)

Observations were made of a patient who was taking a constant daily amount of sodium salicylate by mouth for rheumatic fever and who was maintaining a fairly constant serum salicylate level and then was given sodium bicarbonate to relieve "gastric discomfort". The serum salicylate level fell so decidedly that further investigations of the influence of sodium bicarbonate on the serum salicylate level were undertaken. These latter observations showed clearly that the level is definitely lowered when approximately equal amounts of sodium bicarbonate are given simultaneously. Several factors may be involved (1) interference of sodium bicarbonate with absorption of sodium salicylate in the intestine, (2) alteration of extracellular fluid

leading to a decrease in the titer of sodium salicylate in the blood, or (3) acceleration of the rate of renal excretion of sodium salicylate or its derivatives

Since it is customary to give equal amounts of sodium salicylate and sodium bicarbonate during salicylate therapy, the findings assume considerable clinical importance

## BARBITURATES AND BROMIDES

(Curran, Frank J. Current Views on Neuropsychiatric Effects of Barbiturates and Bromides. *J. Nerv. & Ment. Dis.*, 100: 142, 1944)

In this review of 150 articles in the American and British literature of the past five years, Curran summarises his previous findings and then describes two clinical cases which further substantiate his view as to specificity of bromide and barbiturate psychoses. He points out that in chronic barbiturate intoxication resulting from prolonged use of the medication, there are frank neurological signs similar to those of acute conditions. Drowsiness, difficulties in concentration, disorientation, and euphoria are frequently present, the clinical picture closely resembling general paresis. Of the patients admitted annually to Bellevue Psychiatric Hospital who are diagnosed as having psychoses due to drugs, barbiturates and bromides are the most common etiological factors. The chief treatment consists in stopping the drug, forcing fluids, and giving sodium chloride. In acute barbiturate intoxication the use of picrotoxin is widely recommended. The author reaffirms his conclusion that there is a characteristic clinical syndrome characterising specific drug psychoses, each drug producing a clinical syndrome which differs distinctively from those produced by other drugs.

## INSULIN MIXTURES

(Peck, F. B. Treatment of Diabetes Mellitus by "Single Injection" Method, *West Virginia M. J.*, 40: 341, 1944)

Different patients, being treated by different dietary regimens containing various proportions of carbohydrate, protein, and fat, cannot be expected to respond in a like manner to any single standardized modification of insulin, no matter what modifying agent is employed. The suggestion is made by Peck that it is simpler to adopt a standard dietary system, which does not necessitate special feedings, and to readjust insulin to the case individually than it is to attempt to adjust the patient's condition to a fixed preparation of insulin. The results obtained by such a technic have been briefly summarized, and the method is described. The insulin component of the admixture is determined by postprandial blood-sugar levels and the amount of daytime glycosuria, while the amount of protamine zinc insulin included in the single dose is governed by the blood sugar before breakfast, or the amount of sugar in the urine specimen on arising in the morning.

In general, the proportions of insulin to protamine zinc insulin have varied with the total insulin requirement, although this is not an inflexible rule. Usually, patients who require less than 40 units daily have done well with 3:2 mixtures (3 parts of insulin to 2 parts of pro-

tamine zinc insulin), for those who need between 40 and 50 units daily, the 2 1 mixture is usually suitable, the more severe cases, who need in excess of 50-60 units each day, have required 3 1 or even, rarely, 4 1 combinations

## DIABETIC COMA

(Owens L B The Treatments of Diabetic Coma, Cincinnati J Med, 25 286, 1944)

The term "diabetic coma" has been rather loosely applied to the whole ketosis process, without regard to mental symptoms, although it is better described simply as acidosis or ketosis. The term 'diabetic coma' should be used only with those patients in ketosis in whom the mental state has become one of complete unconsciousness. At the Cincinnati General Hospital, Owens found that the mortality for all degrees of ketosis was 47 per cent. Over 50 per cent of the cases had been in ketosis over sixteen hours and were completely unconscious. The mortality of this group, to which the term "diabetic coma" properly applies, was slightly less than 75 per cent.

A careful study of the case records revealed that the most important factor as associated with a high mortality was the duration of the ketosis before active treatment was instituted.

Early diagnosis and the prompt institution of adequate treatment should take first place. Of all the measures known in combating ketosis, none can take precedence over these. Early and adequate treatment consists of many things. The first and most important is insulin. The second and equally important part of treatment is fluids. These will amount to 4,000 to 5,000 cc in eight to twelve hours. An occasional case is found in which the ketosis is controlled, but in which the carbon-dioxide combining power of the blood does not rise. Soda may be used to advantage in this type of case.

The use of glucose intravenously in the early treatment is not thought necessary. There has been much discussion on this subject. Various clinics in the country disagree as to its need. Some writers believe it does definite harm, in these studies it has been shown that its use prolongs the recovery time, requires more insulin, and that a comparison of mortality there is little difference in those receiving glucose early and those not receiving it at all. Anuria is probably a part of the picture of shock. The greatest hope lies in the prevention of its occurrence by preventing shock or circulatory collapse. The one place left for improvement in the handling of diabetic coma, therefore, is in earlier hospitalization and more prompt institution of treatment. These steps seem imperative if we are to save many of the patients now dying of coma.

## Reflections & Aphorisms

—"When a patient himself complains of auto-intoxication and intestinal stasis, gravely discusses the question of kinks and adhesions, and produces a dairy in which every stool he passes is minutely described, the diagnosis of intestinal hypochondriasis is obvious. The medical profession is, I fear, largely responsible for this common nervous disorder, as these terms are employed too thoughtlessly. The patient must be taught that his auto-intoxication is a result of diugging, that intestinal stasis in moderation is a virtue, as it promotes digestion and absorption of his food, and that we all have kinks and adhesions, and so long as they remain in the abdomen and do not get on the brain they do not really matter."

—"No man knoweth his own bowels, what is good action for one is a poor thing for another, he alone is happy and devoid of that most trying of the nervous disorders of the bowel-intestinal hypochondriasis—who follows Goodheart's, admirable advice to do as the dogs do, and never look behind him."

—"Nervous diarrhoea is a pure neurosis, but rarely a psychoneurosis, and can only be overcome by the regular use of minute doses of drugs which have the power of damping down the gastrocolic reflex, sometimes it is pure hysteria, caused by suggestion, after some strong emotion, maintained by repetition of the emotion, even in a much milder form, and cured by psychotherapy."

—"Muco-membranous colitis is a pure psychoneurosis, requiring but little treatment beyond wholesome neglect." —ARTHUR F. HURST

—"In many cases of psychoneuroses, all one can be sure of is that it would be of little use to try to cure a patient because he needs his illness too much to part with."

—"At the Mayo Clinic the roentgenologists never comment on spasticity, redundancy, kinks, or ptosis. In all such states, they report a normal colon, and they are right, because if the abdomen were to be explored surgically, nothing wrong would be seen. Such findings are often present in 75 per cent of healthy college students and athletes who never have had either indigestion, pain or constipation."

There is not much more reason for blaming a woman's troubles on her low-lying colon than on her low-lying breasts. When one remembers that the progress of material along the intestinal tube is due, not to gravity, but to the wavelike contractions of the muscular coats, it is hard to see why the location of the tube in the abdomen should make any difference in its function. Incidentally, those physicians who talk of faeces weighing down the colon, or being affected by gravity would seem never to have turned around to look in the toilet bowl to discover that this material is so light that it floats in water. Really, since the faeces of the gut have about the same spe-



clific gravity and since this is little different from that of water, they both float in the abdomen together, much like clothes in a washtub full of water"

—"The only possible way in which the colonophobic psychopathic women with irritable bowel can be helped is by explaining patiently to them what the situation is, by casting out fear, and by helping them to learn to live with their unruly bowel. There is no way of curing them so that they will never have trouble again. They must accept their colons pretty much as they are, and they must learn to live with them."

—"Most persons with a sore colon are of a tense, sensitive, nervous, or worrisome temperament. They may be calm externally, but they usually sethe internally, and any strong emotion is likely to affect all those organs which are under the control of the autonomic nerves."

—"The more I see of patients with this syndrome,—'Bowels on the Brain'—the more I am convinced that in many cases the cure could come only if we physicians could get the woman out of a difficult situation, perhaps out of an unhappy marriage or out of a job that is too hard. But often we cannot get her free from the situation that produces her colonic distress, and then we cannot hope to relieve it. I have described some of these situations under the heading of 'the caught-in-a-trap disease'."

—"Often I feel a need for warning the patient not to go ahead and have an abdominal operation performed just because he is desperate, or in a terrible hurry to get well, or unwilling to work hard for his own cure. As the Chinese say, 'There is no sense in trying to escape from a flood by hanging on to tiger's tail'."

—WALTER C. ALVAREZ

# The Indian Physician

VOL IV NO 11

NOVEMBER 1945

WHOLE NO 47

## Original Contributions

### MALARIA IN DISGUISE\*

by

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Although adequate statistics of morbidity and mortality regarding malaria do not exist, it is generally agreed that, apart from the common cold, malaria is the most frequent disease and causes the greatest number of deaths among all existing diseases. Of the 30,00,00,000 cases of malaria occurring every year, 10,00,00,000 cases are found in India (Russell, 1944) and of the 30,00,000 who every year die of it one-third are contributed by this country, it is estimated that in India another two millions every year die of causes indirectly connected with malaria, such as cachexia, anaemia, still-birth and abortion, etc.

Such figures and Sinton's statement that "there is no aspect of life in India which is not affected either directly or indirectly by this disease" might justify it to report some less common aspects of malaria.

*Respiratory System*—Many patients complain about a tiresome, dry, hacking cough, accompanied by fever, which may or may not show the characteristic features of malaria, on examination we find some rales or rhonchi and wheezing sounds just like in ordinary bronchitis. If enlargement of the spleen or routine examination of the blood or a history of periodical profuse perspiration lead us to the diagnosis of malaria, we are sure that anti-malarial treatment will cure this cough which sometimes is the most troublesome symptom in malarial attacks because it disturbs the sleep which the patient needs so badly.

A much more serious condition is pneumonia combined with malaria. In Mysore† we collected 37 cases in one season and here we have seen about 12, where either sulpha drugs brought down the temperature of pneumonias in the course of a day or two but after a short afebrile or subfebrile interval the fever shot up again or sulpha drugs did not act at all on the temperature, although the local signs of pneumonia showed some improvement, and anti-malarial

\* Presidential address delivered at the Annual Meeting Jalpur Branch Indian Medical Assoc., March 3 1945

† Unpublished observation with S K Visveswar

treatment was required to cut short the fever. That is as bad a condition as can be, because our under-nourished, vitamin-deficient people find it hard enough to stand an uncomplicated pneumonia, a superimposed malaria finishes them off quickly unless anti-malarial treatment sets in without delay.

Recently one of our most experienced local practitioners called me to a well-developed and well-fed girl of 11 who was ill for 3 days with moderate fever and under his treatment only for 12 hours, in the morning he found a pneumonic consolidation in the right lower lobe but otherwise her condition was good, he started giving M & B 693. When I saw her the same evening, she was unconscious with a temperature of 105° F and a pulse rate of 160. It seemed unlikely that a comparatively small patch of pneumonia in a strong young girl should not only not respond to proper treatment but even cause such an alarming condition. Without waiting for the result of the blood examination, at 8 p.m. we gave an injection of 7 grains of quinine bishydrochloride, and prescribed 2 hourly oral doses of quinine as soon as she could swallow. At 2 a.m. the girl was conscious and asked for food. The next morning the pathologist reported a heavy M.T. infection. It seems that specially delirious cases of pneumonia which are neither drinkers nor opium addicts should receive early anti-malarial treatment which usually clears up the mental condition in a surprisingly short time.

Applebaum and Shrager (1944) reported 125 cases of malaria in pneumonia, observed in the canal zone of Panama. They seriously consider the question whether a malarial pneumonia exists and come to the conclusion that one group of their cases should be recognized as such, the pneumonic process having been cured by anti-malarial treatment only. Practically of great importance is their experience, fully confirmed by our own results, that sulpha drugs and quinine or atebrin can be used simultaneously without giving rise to any untoward by-effects.

The question whether a malarial pleurisy exists is not decided, although Zimine (1936) reported a case where plasmodia have been found in a pleural effusion. From November 1944 to January 1945, we had a case under observation which fitted into this conception. A well built Rajput male of 35 was admitted with a temperature curve of malarial character, swinging between subnormal and 105° F, profuse perspiration and severe headache. He did not respond to caesalpinia bonducella, plasmodia were not found in his blood although the malaria flocculation test was positive. After a few days, while his general condition quickly deteriorated, an effusion appeared on the left side. exploratory puncture showed a serofibrinous exudate but aspiration did not relieve him at all and sulphapyridine had no effect on the temperature. Under quinacrine (12 tablets) the fever seemed to settle down but after a few days shot up again. His condition became serious and it was decided to try quinine, two intravenous quinine injections of 5 grains each cut short the fever.

which had lasted for more than one month, they were followed by ten days of 20 gr of quinine sulphate orally per day. We kept the patient for another 6 weeks under observation and he remained afebrile throughout, although the pleural effusion was only slowly absorbed and left adhesions behind.

Malaria rarely imitates *heart diseases*, although palpitation and low blood pressure frequently are found as the only symptoms of sub-clinical malaria and sometimes respond well to anti-malarial treatment. But a few weeks ago a much more serious case came under our observation P S (Serial No 6715, 22-10-44 to 3-11-44), an old compounder, was sent by the medical officer of a dispensary outside Jaipur with the diagnosis of coronary thrombosis, based on the history of an unbearable pain in the left side of the chest that had started 3 days ago. In spite of morphine and strict rest the patient became unconscious and, finally, violently delirious so that he broke the needle when his doctor tried to give him another morphine injection for the transport to Jaipur, there was no history of fever. On admission the patient was violent, deeply unconscious, pulse hardly palpable and temperature subnormal, there were no signs of meningitis. Having never seen a coronary thrombosis causing such a mental condition, we started treatment at once by giving 10 grains of quinine intravenous. When we got the report of a heavy M T infection, another 10 gr of quinine were injected the same evening. By this time the patient took some milk and seemed quieter. The next morning he could pronounce his name, under continued anti-malarial treatment he made a good recovery. The electrocardiogram showed no signs of a coronary lesion.

The most common *abdominal* trouble of malarial origin is liver pain that, taken together with liver enlargement which in malarial infections here is almost as frequently seen as enlargement of the spleen—imitates an amoebic hepatitis to perfection. A leucocyte count over 12,000 is in favour of an amoebic infection while enlargement of the spleen points towards malaria, sometimes only the therapeutic test decides.

Malarial attacks occasionally bear all the features of gall-stone colic. I have seen three such cases.

The first was an old Parsee lady in Bombay who was treated for a long time as a recurrent cholecystitis. Her attacks started with a rigor, temperature up to 103° F and an unbearable pain in the gall-bladder region with typical radiation to back and shoulder, the next day she used to be afebrile and entirely free from pain. When I examined her after such an attack, I found not the gall-bladder but the spleen palpable. A course of atabrin cured a long ailment. The next case was a middle-aged man whom we demonstrated in Mysore. The short spell of high fever which completely subsided after one day, the normal leucocyte count and the complete absence of any tenderness in the hypochondrium as soon as the severe colic sub-

sided, led us to the diagnosis of malaria confirmed by a positive flocculation test, after the second attack, which due to anti-malarial treatment remained the last for several years anyhow. The third one was a young lecturer at the Mysore College who was incapacitated for work due to frequent severe biliary colics with fever. A skiagram of the gall-bladder showed a solitary stone of almost 8 annas size. A few days after admission to hospital he developed a typical malarial attack, accompanied by his usual colic. Anti-malarial treatment was started and we demonstrated him in the Mysore Medical Association, more because of the rareness of radio-opaque gall-stones in this part of the country, than because we thought of a casual connection between malaria and his pain attacks. But Dr J F Robinson (then Principal, Medical College and Professor of Surgery in Mysore) pointed out that the gall-stone might have nothing to do with the pain attacks which could be of malarial origin. Fact is that the young man who at the time of the demonstration was fully prepared for an operation remained perfectly well after a prolonged quinine course.

**Case report.**—Another example of the protean character of abdominal malaria is R. B. (Ser. No. 7547, 27.11.44 to 18.1.45) a lady aged 40, who came under our observation with a history of attacks of pain in the right hypochondrium accompanied by hiccough and vomiting, for 6 months, constant pain and anorexia for the last 3 months. After ten weeks of observation in another hospital, an ulcer near the pylorus was diagnosed based on an X ray photo which looked very much like a pyloric stenosis with considerable transverse dilatation of the stomach. A course of 25 Larostidine injections stopped vomiting and hiccough for several weeks whereas the pain persisted. Some time before I was consulted all the complaints recurred, the patient was unable to retain anything, suffered from constant pain and lost about 2 stones of weight. On admission we had to put her on a continuous rectal glucose saline drip. But our investigations failed to confirm the previous diagnosis. Radiological examination of the stomach and the intestines showed normal conditions, a skiagram of the gall bladder to which the localization of the tenderness pointed did not show any radio opaque calculus. Motion and urine were normal. Surprising was the result of two fractional test meals which both showed complete achlorhydria and a very low total acidity throughout. Neither acid mixture nor Pepsindon neither Bellergal Bellafolin nor Spasminidon gave the slightest relief to our patient. seven Larostidine injections were equally of no avail. Finally after 3 weeks of unsuccessful attempts to achieve any improvement her temperature suddenly rose to 101°F with a short shivering. Malaria flocculation test was positive. On the third day of antimalarial treatment she declared to feel better than for a long time, by the end of the course which consisted of 105 gr of quinine sulph. 15 gr. per day, her pain had subsided and light food did not cause any discomfort. After a fortnight a second course of quinine mixture was given and now three months later the patient leads a normal life free from pain, gaining continuously in weight. The most probable explanation of this case seems to be that a chronic sub-clinical malaria caused a pylorospasm of allergic origin.

It is well-known that, especially malignant tertian malaria sometimes causes true dysentery. Such a condition is rare, compared with the frequency of amoebic and bacillary dysenteries. The history of periodic fever and an enlarged spleen together with a considerable amount of dark red or brownish blood in the motions raise the suspicion of malarial dysentery, the four or five cases which I have seen were more dehydrated and emaciated than acute amoebic dysenteries usually are. One or two quinine injections changed the whole clinical picture and the patient recovered with astonishing speed.

Malarial attacks under the picture of acute appendicitis are encountered and cause a good deal of diagnostic difficulties, absence of leucocytosis and a positive flocculation test point to malaria, even if plasmodia are not found.

Of great interest and practical importance are malarial affections of the kidney. *Malcolm Watson* (1904) from Malaya, *Giglioli* (1930) from British Guiana and *Heilig* (1941) from Mysore reported

cases of malarial nephritis. They either present the picture of acute glomerular nephritis or of subacute nephritis, nephrotic type. The first group is accompanied or immediately preceded by acute malaria and quickly cured by anti-malarial treatment, no acute nephritis of any other origin loses albuminuria, haematuria, cylindruria and raised blood pressure in such a short time as a malarial nephritis when treated with quinine. The subacute type which also shows albuminuria, usually a considerable number of red blood cells and casts, further is characterised by considerable oedema and a blood pressure of 130-150 mm Hg with hardly any changes in the fundus. There is no fever or only occasionally a short rise of temperature the spleen is enlarged and the flocculation test usually positive. Typical cases of this group do not respond to anything but anti-malarial treatment, no diuretic acts on them, on the contrary, the anasarca steadily increases, until full doses of quinine are given. Under this treatment some of our cases lost upto 30 per cent of their body weight and the condition of the kidneys improved considerably although usually some traces of albumen and some red blood cells remained as a sign that complete cure can hardly be expected, once the subacute stage of nephritis has set in.

A clinical entity, described by us (Heilig and Visveswar, 1942) is *malarial ascites*, it is not known whether these are cases of late cirrhosis—probably they are, but in the absence of post-mortem findings it is least presuming to call them malarial ascites. All of them have got a big spleen, a very considerable collection of straw coloured ascites fluid of a specific gravity of about 1004, signs of increased intraportal pressure such as collateral circulation and a tendency to haematemesis, there are no signs of renal involvement or of anaemia, blood pressure is normal or low. These cases do not respond to alkaline diuretics or ammonium chloride, very little and only for a short time to mercurials while urea causes toxic reactions, the only way to rid them of their intra-peritoneal fluid was repeated paracentesis. Anti-malarial treatment gives them a fair chance, not of cure, but of fluid elimination by natural ways without loss of proteins which weakens those patients so badly when repeated tapping is done.

There are various *neurological* conditions of malarial origin. The most common are neuralgias which may be localized anywhere supraorbital, brachial and intercostal neuralgia as well as sciatica have been reported which did not respond to any kind of drugs or ray, but completely subsided after a few doses of quinine.

*Epileptiform fits* are seen not only on the height of cerebral malaria but also as equivalents of malarial attacks, occurring at long intervals with apparent well-being in between or such a fit may be the first signal of cerebral malaria even before fever sets in.

Case report. M. C. (Ser. No. 5445 19-44 to 11 9-44), a strong young man of seventeen was brought to hospital deeply unconscious, covered with cold perspiration, he vomited repeatedly, showed collapse temperature and 140 pulse. The history which his father gave was that after two days of moderate afebrile headache which the attending physician traced to some disorder of the liver,

about one hour prior to admission the patient, while making puja suddenly was caught by a tonic clonic fit with conjugated deviation of the eye balls, perfectly imitated by his father, the fit immediately was followed by deep unconsciousness. There was no rigidity of the neck, no Kernig's sign, cerebrospinal fluid was clear though under increased pressure the urine voided by catheter, did not show any pathological changes. In the emergency theatre without waiting for the blood report which soon turned out to be positive for *Pl. falciparum* 10 grains of quinine were given intravenously, two hours later the boy was conscious and the temperature rose from 97° to 101°F. A course of quinine set him right.

This case illustrates the experience which is emphasized by several military medical men, that cerebral malaria not so rarely begins and, if not recognized and treated in the nick of time, ends fatally without showing any rise in temperature. We can safely state that in this part of the country every condition of unconsciousness which is not due to meningitis, pneumonia or poisoning, has to be treated as cerebral malaria, i.e., by intravenous quinine administration.

*Hiccough* sometimes occurs in acute as well as chronic cases of malaria, especially in the latter where no fever indicates its aetiology, it is of real importance properly to diagnose this exhausting condition which, when of malarial origin, does not respond to any other but anti-malarial treatment. Enlargement of the spleen and a positive flocculation test usually point to the right therapy.

*Psychotic conditions* due to malaria have been repeatedly reported, we saw them only in complicating pneumonias, we are using in such cases anti-malarial treatment along with sulphadiazine. It is most gratifying to see how one injection of 5 gr quinine quickly clears up the mental condition, although sometimes high doses of quinine are required to prevent relapses of fever.

One of the most common manifestations of a malarial infection is *myalgia* which usually is localized in the small of the back and the legs, in neck and shoulder muscles or, less commonly, in the chest, as long as those pains are accompanied or shortly followed by fever, there is no difficulty in recognizing their true nature, but if they remain fixed, for instance in a circumscribed part of the abdominal wall, in afebrile cases or still worse, in cases where the temperature chart does not bear any of the characteristic features of malaria, it is very tempting to refer the muscular pain to an organ situated below the tender surface, a wrong diagnosis of appendicitis or cholecystitis happens to be made in such cases. Whether malarial myalgia or myositis is due to trophic impairment, caused by plasmodia obstructing capillaries of the affected muscle, or whether they are of allergic character is difficult to decide.

That malaria may cause *allergic reactions* in predisposed individuals is recognized, whether the allergens are split products of human red blood cells or of malarial parasites is of minor importance. Apart from occasional cases of urticaria, the main manifestations of malaria allergy are painful spasms of smooth muscles such as pylorus, sphincter oddi, caecum etc., and, more important than these, renal damage, appearing in the course of malarial infections. That is at least how we explained (Heilig and Visveswar I c.) the mechanism by which malaria causes and quinine heals or improves

certain cases of nephritis, an explanation accepted by Napier (1942-43)

Finally, we have to remember that every factor which lowers the resistance of an individual tends to cause a flare up of a latent malaria so that fever occurring under such circumstances is likely to be malarial. Such factors are exertion, exposure to extreme temperatures, fatigue, wounds, fractures, deliveries but also common colds, pneumonias and injections of organic arsenicals. In our experience, most of the fever attacks, occurring here after institutional or otherwise well conducted deliveries are due to malaria and not to puerperal infection. One could say, the shorter the interval between delivery and onset of fever, the more severe the rigour and the higher the temperature, the more probable is the diagnosis of malaria. Surgeons in the Middle East, on the Burma front and in the Pacific made thick blood film examination and anti-malarial treatment part of their pre-operative routine.

*Concluding*, one word of caution is indicated. Even the heaviest malarial infection, proved by indubitable evidence, does not exclude the possibility of a co-existing appendicitis, puerperal sepsis or urinary tract infection. In a population, so universally infected with malaria as ours, the probability of double or treble infections is great and to under-rate the actual importance of one of them is a mistake, easily committed. Only by weighing every available evidence against each other, by being prepared at any time to correct a misconception, and by closely following the clinical development, it will be possible to take the right course.

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# INCIDENCE OF AMOEBIC CARRIERS IN BOMBAY\*

by

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During the past 50 years the idea that amoebiasis was a strictly tropical disease and that it usually manifested itself as a fulminating dysentery or a liver abscess has become gradually modified. As epidemiologic studies progressed it was discovered that amoebiasis was practically cosmopolitan in its distribution although its incidence was, as a rule, higher and its clinical expressions more severe in the tropics than in colder climates. Many surveys for the detection of intestinal protozoa have been carried out among military personnel hospital and other institutional inmates and various other population groups in different parts of the world, but none in India. Manson-Bahr (1939) discussing the incidence of amoebiasis and cyst carriers mentions that "there are no reliable statistics for the carrier rate in India, those which are found refer to Indian troops serving in Mesopotamia". I should like, therefore, to describe what I found in Bombay on this interesting subject.

Between April 1939 and October 1942, I was asked to examine 126 persons, all of whom were required to pass a standard of physical fitness. The test was divided into three groups—(1) for physical fitness, (2) for the presence of *Entamoeba histolytica* and ova of parasites and (3) the detection of typhoid carriers. The examination for physical fitness was carried out by me.

In the course of examination each person was asked about his or her family history and his or her own history of previous diseases particularly of typhoid, diarrhoea and dysentery and was subjected to a thorough physical examination, including blood-pressure and urine, and was inoculated against the typhoid group of organism by T.A.B. Vaccine and required to be re-vaccinated before being employed. Those found fit were sent to Dr K T Gajjar M.D., (Lond) for stool examination, and were instructed to take an ounce of Epsom Salts after breakfast and report themselves at Dr K T Gajjar's laboratory at about 10 a.m. The stools were collected in the laboratory and examined within half an hour of voiding. The method used being a fresh saline preparation, an iodine preparation and for ova, concentration. Further the stool was cultured on Mackonkey's medium, the primary idea being to find out the pathogenic bacteria. In the reports mention was made only of *Entamoeba histolytica*, trophozoite form or its cysts, ova of any worms and any pathogenic bacteria grown from the stool but no mention was made of other protozoa considered non-pathogenic. Latterly physical examination as well as stool examination was done by me.

\*A paper read before the 51st Meeting of the Staff Society of Seth G. S. Medical College and K. E. M. Hospital, Bombay, on 11th August, 1945, with Dr N. K. Sahlar, M.D. in the chair.

Of the 126 persons examined only one girl was rejected for being very anaemic and under-weight. The rest were passed as physically fit. In the personal and family histories there was nothing of note. None of them seems to have suffered from any serious illnesses, except one, none ever had had diarrhoea or dysentery. The majority of them gave a history of regular stools. Only two gave statements of having suffered from typhoid fever previously. Not a single case was detected, however, among these 125 individuals of typhoid carriers. All these negative histories may conceivably be due to the over-anxiety on the part of the declarants to secure the jobs they sought and I personally feel they do not deserve implicit credence.

Out of these 125 cases, 67 had some protozoal or parasitic infection giving a total infection of 53.6 per cent, 54 had *Entamoeba Histolytica* in trophozoite or cyst form, giving an incidence in these small series of 43.3 per cent. In all these 54 cases it was the trophozoite form which was noted even though cysts were present in some cases. The presence of *Entamoeba Coli* and other protozoa were not particularly noted and looked for, for reasons explained above. Some however, of the figures recorded are quoted here as being in themselves interesting. *Entamoeba Coli* were detected in 10 cases—in six along with *E. Histolytica* and in four without. *Giardia Lamblia* were present in 3 cases and *Trichomonas Hominis* in one person. Infection with these flagellates was along with that with *E. Histolytica*. In nine cases ova of parasitic worms were found. *Trichuris Trichuria* in 5 (4 per cent), Hook-worm in 3 (2.4 per cent), Thread-worm in 1 (0.8 per cent) and Tape-worm (*Hymenolepis Nana*) in one (0.8 per cent). One case had a combined infection of *Trichuris Trichuria* and Hook-worm. *E. Histolytica* and ova of worms were present together in two cases only. The majority of the 125 persons were young, between the ages of 16 and 25 years, only 13 being above the age of 25 years. The youngest was 16 and the oldest 38 years of age. All of them were unmarried except four women and two men. One hundred and five were women and 20 were men because the factory required more female hands. Ninety-eight belonged to the Anglo-Indian and Christian communities—91 females and 7 males, Nineteen were Parsis—14 females and 5 males, the remaining eight were Hindu males.

Incidence of infection of *E. Histolytica* in relation to sex, community and age (see table) was as follows:

Out of 98 Anglo-Indians and Christians 41 were positive (41.8 per cent), 38 girls (41.7 per cent) and 3 men (42.6 per cent), out of 19 Parsis, 8 were positive (42.2 per cent), 6 girls (42.9 per cent) and 2 men (40 per cent), out of Hindu males, 5 were positive (52.5 per cent). Out of 20 males, 10 were positive (50 per cent) and out of 105 females 44 were positive (41.8 per cent). The average age of 54 positive persons was 21.02 years. From the percentages (even though from statistically insignificant number) quoted above it will be seen that there is hardly any variation between the different communities and sex.

Results derived from the above examinations are of very little statistical value, the number of persons examined being very small. Nevertheless, it is significant that there is such a high incidence of *E. Histolytica* in the stools of young persons who appear otherwise physically fit and do not complain of any symptoms. This incidence, however, is based on one single stool examination. If the stools had been repeatedly examined the incidence would certainly have been still higher (Craig and Faust 1943).

Amoebiasis is probably erroneously classified as a tropical disease. It is specifically a gastro-intestinal disease and is endemic in the whole world. Craig and Faust (1943) estimates a "civilian carrier" incidence of 10 per cent with this communicable parasite in U.S.A. Faust (1942) suggests adequate investigation might approximate a 20 per cent carrier state. In South America and in Mexico the carrier rate is 40 per cent for *E. Histolytica*. In South Africa incidence is at 5-10 per cent (Brink 1943), in England between 5-10 per cent (Manson Bahr 1939), in Norway 2-43 per cent (Boe 1943). It has been prevalent in various parts of Russia at the high percentage of 10 to 30 per cent. Amoebiasis has been present in all the other countries of Europe to a small extent. Incidence of amoebiasis has, of course, been very large in all the other tropical countries. In Ceylon (Manson Bahr 1939), our immediate neighbour, amoebiasis has been prevalent in as high a degree as 75.8 per cent, while in India one always reads of there being a very low incidence of amoebiasis. The only figures which are available on India are those of W. Macadam (1918) giving an incidence of from 5 per cent to 20 per cent amongst Indian soldiers in Mesopotamia, of Danbar and Stephens (1930) of 21.9 per cent amongst South Indians, of Das Gupta and Knowls (1943) of 10.87 per cent in Bengal and of Gharpure and Saldanha (1931) of 7.2 per cent from post-mortem records in Bombay. Tribedi and De (1938) give an incidence from Europeans living in Calcutta of about less than 10 per cent in 1370 stools. If one reads most of the authorities on Dysenteries in India (Acton & Knowls, 1924) (Rogers 1921) one gets the impression that amoebiasis among the civil population is prevalent to a lesser extent in cities than in urban areas, and on the whole it is less than among the Indian troops in Mesopotamia. Faust (1944) in a recent article "Diseases in Tropical War Zones" writes —

"For several decades the Calcutta School of Tropical Medicine has made extensive clinical studies on amoebiasis in Bengal and nearby provinces. Sir Leonard Rogers and his associates called particular attention to the fulminating colitis and liver abscess, types of the disease, and introduced Emetine Hydrochloride as anti-amoebic therapy. In recent years the seriousness of amoebiasis has been less emphasized, although the available data suggest that the disease is no less important than in previous decades. In contrast a more careful study has been made clinically and in Laboratory in differentiating the strains of bacillary dysentery."

Faust, in the same article, without quoting any figures or authorities, considers that the incidence of amoebiasis in Eastern India is high. The figures in the present series justify his conjectures.

As in the present series trophozoites of *E. Histolytica* were found in all cases otherwise perfectly healthy and they might be taken to be just healthy carriers, examples of "Lumen parasitism." According to Reichenow (1932) and Westphal (1938) *E. Histolytica* is normally a harmless commensal, living in the lumen of the intestines, but under certain conditions, found mainly in hot countries, the amoeba becomes a tissue parasite giving rise to pathological condition known as amoebiasis and amoebic dysentery. The factors favouring the passage of the amoeba from the lumen into the tissues have not been determined. Gnezdilov (1943) describes two forms of *E. Histolytica* differing in morphology and in feeding habits, the small commensal (=lumen form) subsisting on bacteria, while the large pathogenic parasites (=tissue form) ingests erythrocytes. The former is called *E. Histolytica forma minuta* and the latter *E. Histolytica forma magna*. Brumpt (1926) had also suggested two similar kinds of *E. Histolytica*. By various experiments on rats (Tuschlya 1939), dogs (Toble 1940) and human beings (Spector 1935) it is now conclusively proved that there is no non-pathogenic variety of *E. Histolytica*. Craig (1936) also says that there are no non-pathogenic races of *E. Histolytica*, but he admits the possibility of a varying virulence and adds that there is no sufficient evidence of permanent immunity after an infection with *E. Histolytica*.

Craig (1935) writes—"It is very doubtful if the term "carrier" should be used at all with reference to infection with *E. Histolytica* if by it we mean an individual in whom the organism is living as a commensal without the production of lesions or symptoms due to its presence."

It is his belief that in every carrier of this parasite cytotoxicity and necrosis of the superficial epithelium in the invaded areas of the intestines is continuously occurring, but when resistance is normal these lesions which are microscopic in size heal rapidly. In some carriers, however, healing does not keep pace with the destructive action of amoeba and ulceration occurs. Presumably tissue invasion takes place even with carriers as these, though not disclosing any symptoms, still show a positive reaction to complement fixation test. Records of numerous autopsies upon individuals who were carriers of this parasite published from time to time, show that not only an extensive superficial necrosis of the mucous membranes of the large intestines but also definite ulceration involving even the muscular coat of small intestines have been present in individuals who had never suffered from diarrhoea or dysentery.

#### SUMMARY

(1) Out of 125 healthy young persons between the age period of 16 and 38 years, 67 (53.6 per cent) had, on one stool examination, protozoal and parasitic infection. Infection with *Entamoeba histolytica*

was present in 54 (43.3 per cent). Even though the number is small there is not much variation in the incidence of infection as regards sex or communities. The average age of the infected persons was 21.02 years.

(2) Not a single typhoid carrier was detected in 125 persons.

(3) The evidence available in the literature shows that even though the *E. Histolytica* carriers as in the case of the above small series, are free from symptoms and are healthy, they cannot but be regarded as definitely clinically infected and treated.

I take this opportunity of thanking Dr. K. T. Gajjar for carrying out the examinations of most of the stools.

TABLE No 1

No	Initials	Sex and		Age	Stool		
		Community			Protozoa	Ova	Culture
1	LM	M.AI		19	Nil	Hookworm	N
10	MES	F.AI		20	E.H.	Nil	N
11	RC	F.AI		25	'	Nil	N
12	EL	F.AI		20	'	Nil	N
15	MO	F.AI		17	'	Nil	N
17	AG	F.AI		17	"	Nil	N
18	AR	F.AI		19	"	Nil	N
19	EB	F.AI		18	Nil	Trichuria T	N
21	NC	F.AI		19	E.H.	Nil	N
24	EM	F.AI		20	E.H.	Nil	N
25	DB	F.AI		18	"	Nil	N
26	IG	F.AI		21	"	Nil	N
27	PKKM	M.H.		21	{ E. Coli Cyst E.H.	Nil	N
28	LH	M.AI		23	E.H.	Nil	N
30	SDD	M.H.		25	"	Nil	N
31	KG	F.AI		18	"	Nil	N
33	SD	F.Ch		20	"	Nil	N
38	GNH	F.AI		27	{ E. Coli Tropho & Cyst Nil	Nil	N
41	KBW	M.H.		25	Nil	T. Trichuria Hookworm	N
42	SNW	F.H.		24	Nil	T. Trichuria	N
43	JC	F.AI		18	E.H.	Nil	N
45	JPk	M.H.		22	"	Nil	N
46	DDM	M.H.		23	" & Cyst	Nil	N
50	TG	F.AI		19	E.H.	Nil	N
51	HLJR	M.P.		20	"	Thread worm	N
52	FBJ	M.P.		25	E.H. & Cyst G.L.	Nil	N
55	RBN	M.H.		22	E.H. & Cyst	Hookworm	N
58	AEB	M.AI		20	EH	Nil	N
60	HM	F.AI		18	'	Nil	N
64	JA	F.AI		20	' + E.C. Troph	Nil	N
65	DW	F.AI		16	"	Nil	N
66	OF	F.AI		18	"	Nil	N
67	NR	F.AI		20	"	Nil	N
69	CF	F.AI		18	'	Nil	N
72	MG	F.AI		18	"	Nil	N
73	BR	F.Ch		23	Nil	T. Trichuria	N
74	PM	F.AI		20	E.H.	Nil	N
75	IJ	F.AI		24	"	Nil	N
79	OC	F.AI		38	E.C.	Nil	N
80	RBK	M.P.		24	Nil	Hymenolepis Nana	N
81	D	F.AI		30	E.H.	Nil	N
82	RBB	F.P.		21	Nil	T. Trichuria	N
84	C	F.AI		32	E.H.	Nil	N
89	EC	F.AI		19	E.C. E.H.	Nil	N
91	DS	F.AI		18	E.H.	Nil	N
96	LC	F.AI		32	"	Nil	N
98	GF	M.Ch		26	"	Nil	N
100	NJH	F.AI		27	"	Nil	N
101	BD	F.AI		19	"	Nil	N
103	IR	F.AI		35	{ G.L. E.C. E.H.	Nil	N

108	NTS	F P	28	E H	NH	N
109	KM	F AI	17	E H	NH	N
111	HJW	F P	19	Trichomonas Homini E.H	NH	N
112	CG	F AI	17	E.H	NH	N
114	GI	F P	24	"	NH	N
115	NVT	F AI	23	"	NH	N
116	NW	F AI	17	"	NH	N
117	BD	F Ch	17	E C	NH	N
118	MG	F P	24	E.H	NH	N
119	M.P	F AI	18	G L, E H	NH	N
122	AM	F AI	18	E.H	NH	N
123	MB	F AI	18		NH	N
124	MTK	F AI	21	E.H E C	NH	N

A I = Anglo Indian  
Ch = Christian  
P = Parsi  
H = Hindu  
F = Female  
M = Male

E H = Entamoeba Histolytica  
Trophozoite form  
E C = Entamoeba Coll  
Trophozoite form  
or cyst  
G.L = Giardia Lamblia

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## INCIDENCE OF CHRONIC AMOEBIASIS IN BOMBAY & NON-DYSENTERIC AMOEBIC ABDOMINAL SYNDROMES

by

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In the course of work in the Out-Patients' Department of the Singhanee Hospital, cases suffering from symptoms pointing to the gastro-intestinal tract were, in the beginning, thoroughly investigated by the following methods—Fractional test meal, Radiological examination of the gastro-intestinal tract following a barium meal, in addition to routine physical examination and stool examination

The results in all these tests were not conclusive and the usual treatment with carminatives and other medicines did not afford the patients more than temporary relief. Some cases, however, with a previous history of dysentery even though the stools were negative for *E. Histolytica*, were treated with anti-amoebic drugs and the results were found to be more satisfactory. In view of these experiences it was decided to lay greater stress on stool examination in investigations of symptoms which pointed to the abdomen. As the results of these stool examinations and symptomatology are interesting I am presenting them here.

During the year 1944, 101 stools of persons attending the Out-Patients Department of the Singhanee Hospital were examined in its Laboratory. These persons mostly described symptoms suggesting affection of the gastro-intestinal tract. The stools in the majority of cases were passed in the Laboratory, following a saline purgative. The majority of cases were examined within an hour or two and the rest within 4 hours of voiding, either by me, by the pathologist Dr S S Kulkarni or by my House Physicians under the supervision of the pathologist. The methods of examination followed were saline, iodine preparation and concentration. The presence of *E. Histolytica* was particularly looked for. Other non-pathogenic protozoa were sometimes not recorded as not being considered important. In practically every case only a single stool examination was done. Let me mention that besides physical examination, stool examination was the only method of investigation carried out in the majority of cases.

The results of stool examination were as follows.

Out of 101 cases, 66 had protozoal or parasitic infection, *E. Histolytica* being present in 58. *E. Histolytica* in trophozoite form was found in 44 and the cystic form in 30 cases. In 14 stools cysts alone were present, in 16 cysts and trophozoite together. Details as regards age and sex in both *E. Histolytica* positive and negative cases are given in Table No I. Of the persons with positive stools for *E. histolytica* the youngest was six months old and the oldest 55 years. Similarity of incidence of amoebiasis as regards age is remarkable in the present series with that of post-mortem series by Gharpure and Saldanha (1931), the highest incidence in both series being in the age group of 20 to 29 years. *E. Coli* was recorded four times. Round-worm in six cases, Whip-worm in three, Thread-worm in one, Ankylostoma in one, Giardiasis in four, *Trichomonas hominis* in fourteen and *Endolimax Nana* in one case.

The symptoms varying in duration from a few days or months to 7 years, complained of by the patients who had *E. histolytica* in their stools were as follows.

- 1 Pain in the abdomen or diarrhoea concurrently or during some time previously.

- 2 Vague pain in the abdomen, mostly in the epigastric region, either in the right iliac fossa or in the left iliac fossa.

3 Opening of the bowels twice or thrice a day Stool varying in character from semi-solid to watery and sometimes explosive, preceded, by griping pains on the left side of the abdomen Mucous in some cases, and in others, a feeling of the rectum not being completely empty, this feeling being described by them as "constipation" In point of fact, some do really suffer from constipation while others from constipation alternating with diarrhoea

4 Flatulence and discomfort in the abdomen, particularly in the epigastric region and on the left side Eructation and belching, vomiting and hiccough

5 Low fever, aches all over the body, lassitude, headache and giddiness

6 Poor appetite, stomatitis and aphthous ulcers in the mouth

7 Pain in the chest, in the back, between the shoulders and nervousness, apathy, listlessness and lack of zest

8 In the case of females, irregular monthly periods and excessive leucorrea

9 Loss of weight

Only five in the whole series gave a history of previous attacks of dysentery

Some cases were found on examination, to be slightly anaemic, the majority a bit thin, some normal and some stout Stomatitis, glossitis and aphthous ulcers were present in the mouth Abdominal examination showed the colon to be palpable, generally on the left side, the caecum in many cases palpably thickened, there being sometimes gurgling, discomfort and tenderness over it

The following are the symptom complexes (syndromes) of some of the patients which simulate various other conditions

1 The Patient complains of low fever daily for one to two months, or for a few days at frequent but irregular intervals The maximum temperature is usually never more than 100° F in the evening and normal in the morning Occasionally, however, he runs a temperature the whole day The symptoms include poor appetite, malaise, headache, general tiredness accompanied by distention of the abdomen, notably in the epigastric region These attacks of distention and fever come on sometimes separately, at other simultaneously Such patients have usually no pain in the abdomen, diarrhoea or stomatitis They are erroneously treated for early tuberculosis of undermined site

2 Some patients complain of vague pains in the abdomen, usually located round about the umbilicus, more pronounced towards the left side, and of having one or two and sometimes three stools in the course of the day Each stool, however, leaves them with a feeling of having had only a partial evacuation of the rectum with the result that they are liable to strain in trying to effect complete evacuation and thus produce such harmful consequences as a development of



prolapse of the rectum or hernia. They are however, free from symptoms for the rest of the day. These types of patients often complain of constipation.

3 Quite a number of patients complain of symptoms simulating peptic ulcer. Others have a feeling of fullness and the majority pain after food in the region between the epigastric angle and the umbilicus. The pain is usually in the middle and at times on either side. It comes on in most cases either immediately or within half an hour after food, but it also does occur any time from between a few minutes to as late as four hours after meals. Although there is, in some cases, a history of remissions and intermissions, the characteristic clock-like regularity of the pain of peptic ulcer at a localised spot is absent. The pain recurs in the evening, quite often between 7 p.m. and 9 p.m. but it very rarely disturbs the patient at night, as in the case of typical peptic ulcer. Patients usually drop their evening meal because of their fear of pain. The pain or feeling of fullness in these cases is usually due to the pressure of a full stomach on the distended transverse colon.

4 Others complain of symptoms resembling chronic appendicitis. In such cases the predominant symptom is constant recurring pain, in right-iliac fossa, either present the whole day, or intermittently, and brought on, or augmented by ingestion of food or by certain kinds of food. It may be acute, colicky, or it may take the form of a continuous dull but not severe ache. There may be, in addition, a feeling of general fullness and ache or malaise in the whole of the abdomen, particularly in the left iliac fossa or in the hypochondrium without any previous history of diarrhoea or dysentery. There may be a previous history of such attacks of pain on the right side. There may or may not also be diarrhoea with or without blood or mucous. The most difficult cases to diagnose are those in which the stools are normal as in these the temperature is mostly normal and only occasionally rises to 100° F. On examination a slight prominence might be found in the right iliac fossa and tenderness over the McBurney's point. This may also be present above or below it and more often over the caecum which is palpable. Both the thickening and gurglings over the caecum are present in the majority of cases of chronic amoebiasis. Such cases are often treated and operated on as cases of chronic appendicitis or tuberculosis of the caecum.

5 The pain in the abdomen may be connected with a history of alternating constipation and diarrhoea and the occurrence of glossitis and aphthous ulcers, often complained of, is found to coincide particularly with the period of constipation.

6 In women vague pain in the abdomen at any time during the month becomes much more acute at the time of the monthly periods and remains very severe not only at the beginning but throughout the monthly periods. The periods are often irregular and there is in the interval an excessive amount of leucorrhoea, probably due to general debility and anaemia which follow chronic amoebiasis.

Such patients, notably if they are young and nulliparous women, are treated as cases of dysmenorrhoea

7 Pain on the left side of the abdomen in two cases was so severe that it simulated renal colic, it being of an acute colicky nature localised in the left lumbar region and at the back and accompanied by nausea and frequency of burning urine. Urine examined was normal during the attack, but the stool showed the trophozoite form of *E. histolytica*. The patients were relieved of this symptom by treatment for amoebic dysentery.

8 The patient who was formerly in perfect health finds that over a period of years he has become highly strung, nervous, irritable and easily susceptible to fatigue. He is, moreover, lacking in ambition and if he holds a responsible position may find it ultimately necessary to give it up. Abdominal symptoms are usually limited to discomfort in the form of sharp shooting and variously located pains. Such a patient will have consulted many physicians and his condition is diagnosed as neurosis of undetermined origin.

Amoebiasis is recognised in its chronic forms to a lesser extent than in its other manifestations (a) acute form of dysentery or (b) liver abscess (Craig & Faust 1940). Rogers (1944) mentions diarrhoea without blood and mucous and occasionally tenesmus as symptoms of the chronic form and warns that it may be mistaken for simple or tuberculous diarrhoea. Faust (1944) writing about India says "in recent years the seriousness of amoebiasis has been less emphasized," but Payne (1945) in his observation of 2000 cases of dysentery in Eastern India remarks that amoebiasis is  $1\frac{1}{2}$  times as common and is more serious as regards morbidity than bacillary dysentery. One observes that morbidity, caused by chronic amoebiasis is not sufficiently realised and with this point in mind the symptoms and symptom complexes (syndromes) noticed in this series are presented.

#### SUMMARY

1 Of the 101 persons with abdominal symptoms whose stools were examined, 66 showed the presence of protozoal or parasitic infection, 58 having *Entamoeba histolytica*.

2 The symptoms complained of by these patients have been enumerated and emphasised.

3 Attention is drawn to the fact that chronic amoebiasis is much more prevalent than is imagined and is responsible for chronic, though not serious ill-health to a larger extent than is generally realized.

I take this opportunity to thank Dr S. S. Kulkarni, the pathologist and my House Physicians Drs S. H. Shah and Pandya for their help in stool examinations. I am also grateful to Dr R. Roy, Hon. Director P. G. Singhania Hindu Hospital for his guidance throughout the period and for allowing to publish this paper.

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Table No I

Age in Years	Total Cases	Male Female positive		Male Female negative		
0 months—9	8	5		3		62 5%
		M	F	M	F	
		4	1	1	2	
10—19	11	7		4		63 6%
		M	F	M	F	
		2	5	1	5	
20—29	33	23		10		Highest Incidence
		M	F	M	F	
		11	12	7	3	60 6%
30—39	32	15		17		
		M	F	M	F	
		12	3	12	5	46 8%
40—49	13	7		6		
		M	F	M	F	
		5	2	4	2	53 8%
50—59	4	1		3		25%
		M	F	M	F	
		1		3		
	101	58		43		
		M	F	M	F	
		35	23	28	15	

## DISCUSSION

Major P V Gharpure speaking about the incidence of amoebae in the stools said that in his experience it was about 12%. In a careful examination of the stools in 970 men 50 showed the cystic forms but in none of them could the trophozoites be demonstrated. The latter forms were seen by him only in cases with diarrhoeic or dysenteric symptoms.

With regard to the incidence of typhoid carriers he referred to the work of Mackenzie (J of Hygiene 1945 Vol 44 No 1) who examined the stools in cases giving a positive Vi agglutination test in the blood. In not a single of these cases could the organism be isolated from the stools. In connection with the carrier state he mentioned that in an examination of the coecal contents carried out at the autopsy, he was able to demonstrate viable eggs of the house fly in 50% of the cases. He agreed with the speaker that chronic amoebiasis can simulate various other diseases.

Dr L Monteiro referred to the stool examinations carried out in the Department of Pathology during 1944. Of a total of 817 stools examined 103 showed E histolytica including 6 where the trophozoites were seen. In addition the following were detected —

Cysts of E coli	17
„ of G lamblia	23
T hominis	3
Ova of A lumbricoides	110
of A duodenale	72
of T trichlura	94
of O vermicularis	3
of T saginata	3

He further observed that these stool examinations were carried out in hospital patients suffering from some abdominal disturbance or the other. In spite of this, the incidence worked to be about 12.5%, a figure that compared with that of Das Gupta and Knowles (10.87%) in Calcutta. He further added that in diagnosis of chronic amoebiasis repeated stool examinations were necessary as cysts are passed intermittently. It was therefore very creditable that Dr J C Patel was successful in demonstrating the parasite in such a high proportion of cases.

Dr P Raghavan said 'I congratulate Dr J C Patel for bringing to our notice the great frequency of amoebiasis in people who are apparently healthy and in those with vague abdominal symptoms. The practitioner is conscious of the nature of acute dysentery or manifest hepatitis. But what is

more important is to realise the variety of ways in which chronic amoebiasis as contrasted with amoebic dysentery can masquerade. Some of these patients may have forgotten a distant episode of diarrhoea and abdominal discomfort they may have had. When a patient comes to us with unexplained, vague abdominal symptoms which may go under the term neurosis or low grade pyrexia or general ill health besides doing other things one has to examine the second or third liquid stool after the administration of a cathartic carefully for triphozoites and cysts of *Entamoeba histolytica*.

It is interesting to note that a number of these patients lose the zest for life and complain of lack of energy. It is known that anxiety states are reflected in disturbances of bowel function but I do not know whether the ulcerative conditions of the bowel can precipitate an anxiety state.

Dr K A J Lalkaka said that with regard to symptoms of psychoneurosis, there were two distinct types of cases, one, in whom the psychoneurotic reaction was the result of amoebiasis and the other where colitis was due to the psychoneurosis.

Dr R G Dhayagude agreed with Major Gharpure that the incidence of amoebiasis cited amongst young healthy individuals by Dr J C Patel was much more than what his experience was. An investigation of the stools of the staff working at the Dadar sewage purification was carried out in the Pathology Department and it was found that about 3 to 4 persons showed cysts of *Entamoeba histolytica* amongst a group of 46 employees. He suggested a survey on a large number of healthy individuals in view of Dr Patel's findings. He quoted his own experience where in some cases of low fever, loss of weight, and sweating, in which symptoms suggested a diagnosis of tuberculosis a stool examination was carried out and cysts of *E. histolytica* were detected. The subsequent report in those cases was that they were cured of their symptoms on receiving treatment for amoebic infection.

In replying Dr J C Patel mentioned that he was convinced in every case as to the presence of cysts or trophozoites in the stools. He agreed with Prof R G Dhayagude that a larger survey was necessary and suggested that it might be carried out in the medical and nursing students of the institution.

## CALCAREOUS PANCREATITIS

### AUTOPSY REPORT OF ONE CASE

by

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Stone formation in the pancreas was first recognized in 1661 by Graaf Morgagni in 1765 and Cawley in 1788 reported autopsy findings of calculous pancreatitis. Cawley's case was associated with diabetes. In 1901 Opie stated that stones may lead to atrophy of the pancreatic parenchyma.

Mayo in 1936 reported 25 cases of pancreatic stones—in the Mayo Clinic. In the next 4 years Snell and Comfort detected 18 cases. This increase in incidence of pancreatic calculi since 1925 is probably due to more frequent roentgenological examination of the abdomen.

*Autopsy Report*

*Clinical notes*—A Christian male aged about 50 years admitted for the following complaints (1) Polyuria, (2) Polydipsia, (3) Pain and weakness in the lower extremities—duration 2 months.

Two months prior to these complaints he had fever for two days only and after that he noticed frequency of micturition, the D/N micturition ratio being 6/8.

*General Examination*—Showed an emaciated individual, nails and conjunctivae pale and the lower limbs were covered with a scaly eruption.

*Systemic Examination*—Tongue was dry, liver and spleen not palpable. Heart N.A.D. B.P. 105/75 mm of Hg. C.N.S. motor and sensory systems were normal. Superficial reflexes were normal. Deep reflexes present but sluggish. Chest Signs of pulmonary infiltration.

**Laboratory Investigations**—Routine examination of urine showed presence of sugar, no other abnormal constituent detected Blood sugar tolerance curve showed the following figures

Fasting sample	210	5 mgm/100 c.c of blood	
$\frac{1}{2}$ hour sample	296	6 mgm	"
1 hour sample	400	mgm	"
$1\frac{1}{2}$ hours sample	444	4 mgm	"
2 hours sample	500	mgm	"

Sputum showed M tuberculosis by ordinary method Erythrocytic sedimentation rate was 92 mm at the end of one hour (Westergren's method)

**Treatment**—He was put on a restricted diet and treated with Ameiline powder Urine samples tested 3 hours after meals showed marked fluctuations in sugar contents during the course of the treatment No history of diarrhoea or pain in the abdomen was available He expired 4 months after admission

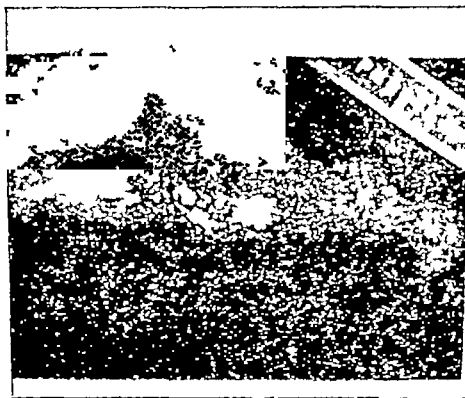


Fig 1

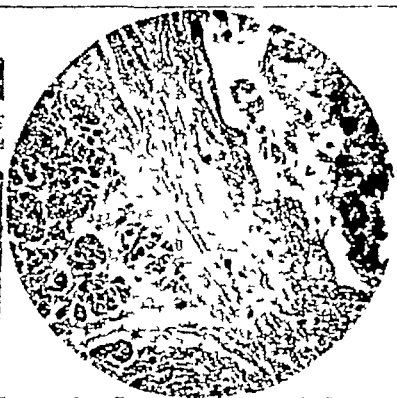


Fig 2

The following findings were seen during the autopsy examination

He was well-built but emaciated, nails and conjunctivae were pale On opening the body both pleural sacs showed fibrous adhesions and the left pleural sac contained about 50 c.c of straw coloured turbid fluid with flakes of fibrin Omentum was markedly congested and covered with numerous tubercles Serosal aspect of the small intestine also showed similar tubercles Coils of the small intestine were adherent to each other and were covered with fibrinous exudate

**Alimentary System**—Tongue pale and showed atrophic glossitis, stomach mucous lining showed atrophy and pallor Typical tuberculous ulcers were present in the ileum Large intestine did not show any abnormality

**Liver**—Small (750 gms) and firm Fine yellow tubercles were seen on the surface and in the substance of the liver Liver parenchyma showed a cloudy degeneration Gall-bladder was smaller than normal, contained golden yellow coloured bile and its mucosa was normal No gall stones detected C Bile duct was also normal

*Pancreas*—It was shrunken and several calculi were palpable in its substance, more so in the head. The feel of the organ was that of a bag of stones (fig 1). It weighed 52 grams and measured 15 cms by 5 cms. On dissecting a part of the main pancreatic duct, calculi could be seen in the dilated lumen. One such calculus was removed for detailed examination. It was about  $\frac{1}{2}$  cm by  $\frac{1}{4}$  cm, irregularly oval in shape, its surface was rough and whitish brown in colour. Its consistency was hard and chemical qualitative analysis showed it to consist essentially of calcium carbonate, traces of calcium phosphate and organic matter. Histological examination (fig 2) showed distortion in normal lobular and acinar structures by proliferating interstitial connective tissue. The lobules were of varyign sizes and shapes, with intervening thick fibrous septa. Some showed atrophic changes. Interacinar connective tissue was also increased. The ducts were distorted and one of them showed marked dilatation with desquamated, necrotic lining cells and concretions. No evidence of squamous metaplasia of the duct epithelium was seen in these sections. Islets of Langerhans were diminished.

*Respiratory System*—Both lungs showed fibrocaseous tuberculosis and tuberculous broncho-pneumonia. Histological appearance from these lesions confirmed the morbid anatomical diagnosis.

*Circulatory System*—Heart, well marked brown atrophy. Aorta early atheromatous change.

*Genito-urinary System*—Right kidney showed a minute tuberculoma in the interpyramidal cortex and a fibroma in one of the pyramids. Left kidney did not reveal any tuberculous lesion in the substance. Testes, prostate and bladder normal.

*Haemolymph System*—Spleen was small and firm with areas of perisplenitis. Histologically small tubercles were detected in the substance. Mesenteric lymph nodes and lymph nodes round about the pancreas showed evidence of caseation.

*Central Nervous System and Endocrine System*—Normal.

*Incidence*—In the first five thousands autopsies performed in this institution, there were 38 cases showing various lesions in the pancreas. Only one case showed stones in its substance.

Opie has reported only two cases of pancreatic calculi in a series of 1,500 necropsies. Dillon during 2,800 autopsies came across pancreatic calculi only twice. As opposed to these figures suggesting rarity of the lesion Ludin by careful examination in 542 autopsies demonstrated calculi in 28 cases. Warren described 3 cases of calculi in a series of 300 autopsies performed on diabetic patients. Shah reported two cases of pancreatic lithiasis in 1941 before this society, one manifesting diabetes mellitus and the other renal type of glycosuria.

*Pathogenesis*—Various factors have been held responsible in the production of this condition. The predisposing condition is cholelithiasis with subsequent infection of the pancreatic ducts. This probably leads to stasis which brings about alterations in the pancreatic

juices resulting in deposition of calcium Tuberculous lesions and acute focal necrosis have also been held responsible especially in cases where the calculi were found in the parenchyma These concretions can occur either in the ducts or in the parenchyma They may be sandy or gravels They are often mixed with organic matter As the lesion progresses, atrophy and fibrosis of acinar tissue occurs first and the Islets of Langerhans are not significantly involved until the disease is far advanced

**Diagnosis**—Important symptoms include attacks of acute pain in the upper abdomen, steatorrhoea and sometimes glycosuria

Radiology has a very definite place in the diagnosis of pancreatic lithiasis

Laboratory investigations useful in arriving at a diagnosis in such cases are the following

- 1 Examination of duodenal content for constituents of pancreatic juice  
Amylase and lipase are deficient in such cases
- 2 Chemical quantitative estimation of fat in stool  
In pancreatic diseases unsplit fats constitute about 40 to 70 per cent of total fats
- 3 Lastly in cases showing glycosuria a glucose tolerance curve is useful

The most debatable point in such pancreatic lesions is its relation to diabetes mellitus No definite co-relation of sclerosing lesion in the pancreas and diabetes has yet been established It is a well-known fact that very few islet cells are necessary to maintain normal carbohydrate metabolism According to Warren one case of stone in the pancreas in hundred diabetes, is not conclusive evidence as to the role stone formation plays in production of diabetes It is possible that sclerosing lesion may ultimately lead to diminution of islet tissue resulting in diabetes

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#### DISCUSSION:

Dr Z J Joseph demonstrated skiagrams of two cases of pancreatic lithiasis discovered accidentally during the course of his work.

Dr A Hameed said that the case reported by Dr Kothare had not been investigated for pancreatic calculi as the patient did not have symptoms suggestive of pancreatic disease Treatment with amellin claimed to be an anti-diabetic drug was unsuccessful as the patient died of generalized tuberculosis

The second case referred to by Dr Joseph, was of an unmarried girl, 27 years, emaciated and anæmic Pancreatic calculi, gastroptosis and a movable kidney were present. Urinary diastase was 20 units, fasting blood sugar 129 mgms/100 c.c., and the faeces did not show excess of fat The patient could not be followed but the interesting point was that inspite of the calculi, pancreatic function as could be judged by investigations carried out, was unimpaired

Dr L H Athale observed that pancreatic calculi were often discovered accidentally in skiagrams and these cases were not always accompanied by symptoms suggestive of pancreatic disease

Dr R G Dhayagude said that the object of presenting the post mortem findings of the case of Pancreatic Lithiasis was to bring home to the members of the staff the fallacy which might arise in investigations if adequate care is not taken to exclude concomitant findings which might vitiate the diagnosis This case was taken up for the trial with Amellin on a supposition that it was a clear cut case of diabetes mellitus When such a large number of calculi were present in the pancreas and the fibrosis of pancreas was so evident it is possible that the diabetic condition might be secondary to calculous pancreatitis. The case was therefore unsuitable for this particular type of investigation

This also raised the issue whether it would not be considered advisable to undertake radiological investigations in such cases.

# The Indian Physician

VOL IV NO 12

DECEMBER 1945

WHOLE NO 48

## Original Contributions

### URAEMIA

AN ANALYSIS OF 98 CASES ADMITTED TO THE K E M HOSPITAL  
FROM 1st JANUARY 34, TO 30th JUNE, 44 WITH  
POST MORTEM FINDINGS OF 36 CASES

by

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Kassanji Ranchhodji Desai prize essay for year 1944.

The word uraemia literally means urine in blood, and was coined by Piorry to designate an intoxication resulting from insufficient depuration of blood by the kidneys. The criterion whether a symptom complex, occurring in a patient with kidney disease is a manifestation of uraemia or not, is its obligate connection with renal insufficiency, and we may define uraemia as a symptom complex resulting from renal failure and accompanying the retention of urinary constituents in the organism.

*Occurrence of Uraemia*—Uraemia can occur as a result of any of the manifold processes that inhibit the formation of urine, or its transit along the urinary passages. The causes of uraemia fall into three groups.

1 *Pre-renal Uraemia*—Here nitrogenous retention occurs as a result of decreased blood flow through the kidneys—described as uraemia with histologically intact kidneys. It occurs in conditions like severe and protracted vomiting and diarrhoea, diabetic acidoses, crises of Addison's disease, shock and collapse, severe wide spread burns, profuse haemorrhage from gastro-intestinal tract etc.

2 *Renal Uraemia*—Any disease of the kidney in which a large part of renal parenchyma is destroyed so that, the remainder is unable to compensate for it, culminates in uraemia.

3 *Post-renal Uraemia*—This occurs as a result of obstruction of urinary passages.

The aim of this paper is to study from clinical point of view, all the cases of renal uraemia admitted to the K.E.M Hospital, Bombay, during the period 1st January, 1934 to 30th June, 1944, i.e., all cases admitted in last ten years and six months. There were 98 cases during this period and an analysis of these cases is given below. During



the same period total number of in-patients treated in the hospital on medical side was 55,839, so that uraemia cases formed 0.17 per cent of total number of admissions on medical side, or in other words, for every 588 cases admitted on medical side there was one case of uraemia. The yearly incidence of uraemia shows that the incidence was greater in the years, 1934 (0.23 per cent), 1936 (0.34 per cent), and 1942 (0.23 per cent) and was low in the years 1935 (0.10 per cent), 1940 (0.10 per cent), and 1944 (0.11 per cent). In the remaining years it is fairly constant and compares favourably with the collective percentage.

**Age**—The youngest age at which uraemia occurred in the present series was 2 years, while the oldest case was 81 years old. 75 per cent of cases were between the ages 21 and 60. The maximum incidence in the ten year group being 23 cases between 21 and 30 years—the second highest being 22 cases between 31 and 40 years. The details of the age incidence is shown in Table 1.

Table 1 Age incidence in uraemia

Age	No. of Cases	Percent	No. of Cases	Percent
1—10	7	7.14	16	16.32
11—20	9	9.18		
21—30	21	23.47	45	45.92
31—40	22	22.45		
41—50	10	10.39	30	30.02
51—60	11	11.23		
61—70	5	5.10	7	7.14
Above 70 years	2	2.04		
Total	98	100.00	98	100.00

On plotting a curve of age incidence in uraemia, we find that the curve shows a steep rise at a period between 21 and 30 years and a gradual fall throughout.

**Sex**—In the present series there is a definite preponderance of males over females. Out of 98 cases, 69 were males and 29 were females. But this is more apparent than real because these figures are taken from a hospital where there is a remarkable preponderance of male admissions over female admissions on medical side and so these figures are compared to male and female admissions into the hospital on medical side in Table 2.

Table 2 Sex incidence in uraemia

	Total	Males	Females	Male %	Female %
Uraemia cases	98	69	29	70.4	29.6
Admissions on Medical side	55,839	11,120	1,111	77.8	22.2

From the above table, it is evident that incidence of uraemia is slightly more in females than in males.

The annual sex incidence shows that incidence in females is higher in years 1936 (47.1 per cent), 1939 (50.0 per cent), and 1942

(41.7 per cent), whereas that in males is higher in the years 1935 (100.0 per cent), and 1940 (100.0 per cent). In the remaining years, it is fairly constant and compares favourably with the collective sex incidence.

The following table shows sex incidence at different ages.

Table 3 Sex incidence at different ages

Age	No. of Cases	Males	Females	Male %	Female %
1—20	16	8	8	50.0	50.0
21—40	45	35	10	77.7	22.3
41—60	30	22	8	73.3	26.7
61—80	7	4	3	57.1	42.9
Total	98	69	29	70.4	29.6

From this table we find that incidence in females is relatively higher at the extremes of life i.e., in the first 20 years of life and from 61 years to 80 years and above, than that in males in whom the incidence is greater between the ages 21 and 60 years.

**Community**—Here we find that there is a marked preponderance of uraemia in Hindus as compared with others. 61 out of 98 cases were among Hindus. This is apparent rather than real because the number of Hindu admissions far exceeds the number of admissions to the rest. Comparing the percentage of uraemia cases in different communities with the percentage of their admissions, we find that incidence is slightly less in Hindus than the rest. How far this may be due to their diet differences, is very difficult to say because notes as regards their diets are very scanty. The following table shows the incidence of uraemia in different communities.

Table 4 Uraemia in different communities

	Total	Hindu	Moslem	Christ	Parsis & others	Hindu %	Moslem %	Christ %	Parsis & others %
Cases of Uraemia	98	61	20	14	3	62.2	20.4	14.3	3.1
Total Hosp. admissions	133,001	91,027	20,875	18,005	3,397	68.0	15.6	13.0	2.5

**Occupation**—Out of 69 males, occupation was not known in 25 cases. In the remaining 44 cases, the occupations were as follows.

Occupation	No. of Cases
Clerks	9
Mill hands	8
Domestic servants	6
Students	4
Farmers	4
Hawkers	4
Masons	2
Mechanics	4
Carpenter	1
Cardener	1
Tailor	1
Total	44

**Renal diseases**—Incidence of uraemia in different forms of renal diseases varies greatly. In chronic glomerulo nephritis, uraemia is common, being the most frequent cause of death. In acute glomerulo nephritis, it is not as common as in chronic form. It is an invariable

ending in the malignant form of hypertension, and is not at all uncommon in bilateral suppurative disease of the kidneys and usually terminates polycystic kidneys. In the present series of 98 cases, 45 cases were due to chronic glomerulo nephritis. The incidence of uraemia in different forms of renal diseases is given below.

**Table 5** Incidence of uraemia in different forms of renal diseases.

Different kidney diseases	Uraemia Cases
Chr. Glomerulo nephritis	45
Nephrosclerosis	12
Acute nephritis	8
Pyelonephritis	7
Hydronephrosis	4
Sub-acute Nephritis	2
Polycystic kidney	2
Unknown	18
Total	98

In 18 cases written as unknown in the above table, it was not possible to find out from the notes as to whether they belonged to acute nephritis, chronic nephritis or nephrosclerosis.

**Clinical Manifestations—Onset**—The onset is usually, though not invariably, insidious. There is often a latent period between the beginning of renal insufficiency and the onset of uraemia symptoms. Out of 98 cases, 26 cases were admitted in an unconscious condition and no proper history was available. In the remaining 72 cases, there were varied initial symptoms like mental and physical fatigue, loss of weight, anaemia, gastro-intestinal symptoms, and nervous symptoms like apathy, drowsiness and headache. These symptoms were elicited after the diagnosis of uraemia was made in some of the cases. It is also important to note that any infections, febrile conditions or any interference in the genito urinary tract might precipitate uraemia in a patient who might be suffering from renal disease. Out of 98 cases uraemia set in 12 cases as a result of some such factors e.g., fever with rigors with enlarged spleen was responsible for five cases. Post-mortem in one of these cases showed evidences of chronic nephritis. Tonsillitis was responsible for 3 cases, scabies, nephrectomy on a hydronephrotic kidney, appendicectomy, and operation for phimosis were each responsible for one case of uraemia. Post-mortem examination in the last two cases showed the evidences of benign nephrosclerosis and acute exacerbation on chronic nephritis with staphylococcal abscesses in kidneys due to staphylococcal pyaemia respectively.

As said before, symptoms of uraemia are very varied and all the systems of the body may be affected equally or one system may be affected more than the other. Unless the possibility of uraemia is kept in mind it is likely to be mistaken for any disease of the various systems affected. In the present series of 98 cases, all systems were affected. In addition, haemorrhages, skin affections, and generalised anasarca were seen in some of the cases. The following table shows the extent to which various systems were affected in the present series.

Table 6 Incidence of affection of different systems

System affected	No of Cases	Percentage
Nervous	98	100 00
Cardio vascular	62	53 06
Respiratory	43	43 86
Alimentary	72	32 64
Generalised anasarca	60	61 02
Genito-urinary	27	27 54
Haemorrhages	28	28 56
Skin eruptions	3	3 06
Total	98	100 00

*Nervous Symptoms*—Initial symptoms were those of mental and muscular weakness leading to reluctance on the part of the patient to carry out any mental or physical work. Patients were apathetic, complaining of weakness and a constant feeling of drowsiness. Despite the mental torpor, there was often extreme physical restlessness. All patients had these symptoms sometime or other.

All patients became unconscious at the end but 26 cases were admitted in an unconscious condition, some with the mistaken diagnosis of meningitis, encephalitis, tetanus, cerebral malaria, narcotic poisoning etc. True diagnosis was established by proper investigations and in some cases only on post-mortem examination.

Dull headache occurring in any part of the head is a frequent, quite often initial but not a constant symptom of uraemia. It was present in 14 cases only. Table No 7 shows the relative occurrence

Table 7 Nervous symptoms in uraemia

Nervous symptoms.	No of Cases
Drowsiness, restlessness, delirium, etc.	98
Admitted unconscious	20
Headache	14
Muscular twitching and convulsion	14
Mental symptoms	11
Paralysis	10
Blindness	3
Total	98

of nervous symptoms in uraemia. Muscular twitchings in the form of fibrillary twitchings were noted in 14 cases, out of which 9 cases ultimately got generalised convulsions. They were present in but 2 of 51 cases of uraemia studied by Oppenheimer and Fishberg. True uraemic convulsions are generally not as violent as the full blown epileptiform convulsions, that manifest the non-uraemic hypertensive encephalopathy, which is always accompanied by sudden rise of blood pressure.

Mental symptoms in 11 cases consisted of transitory or permanent mental disorientation, depressive or excited states. Two of these cases were diagnosed as (?) Hysteria, (?) Insanity.

Paralysis in 9 cases consisted of hemiplegia and in one case of monoplegia. Post-mortem examination was held in 7 cases, out of which, gross lesion was detected in 2 cases only—Intra-cerebral haemorrhage occurring as a complication of hypertension in one case, and thrombosis of middle cerebral artery in the second case. In the remaining

5 cases there was atheroma of the vessels of circle of Willis or oedema of brain. No gross lesion was detected to account for widespread paralysis. These local palsies, hemiplegia or monoplegia may come on spontaneously or after a convulsion and are frequently due to small vascular lesions. In the present series of 98 cases, 10 cases, that presented paralysis, did not have any convulsions at all, and so these were not the cases of Todd's paralysis occurring after convulsions.

Blindness was present in 3 cases and retinal examination showed albuminuric neuro-retinitis, consisting of exudates and haemorrhages in the retina and papilloedema of the disc. The arteries were thinned out and the veins were engorged and tortuous. In one case in addition to above changes, there was exudative detachment of retina in one eye.

**Cardio-Vascular Symptoms**—Almost all varieties of renal disease that lead to uraemia, are associated with hypertension and cardiac hypertrophy. Exceptions are mercurial necrosis, amyloid contracted kidney and renal failure supervening on subacute nephritis. Blood pressure may drop because of cardiac weakness, but cardiac enlargement reveals antecedent hypertension. Post-mortem will show hypertrophy of the muscle of left ventricle. In this series blood pressure was recorded in 76 cases, out of which 45 cases showed high blood pressure varying from 160 to 290 mms of Hg systolic and 100 to 170 mms of Hg diastolic. The remaining 31 cases showed normal blood pressure. Post-mortem examination was held on 10 cases out of 31 cases with normal blood pressure. Four cases showed antecedent hypertension by the presence of left ventricular hypertrophy. In one case the heart was not opened and the remaining 5 cases did not show any hypertrophy of the ventricular walls. These 5 cases had the following kidney diseases:

One case of each of—Subacute nephritis, Pyelonephritis and amyloid contracted kidney, Ascending pyelonephritis, Chronic nephritis, Polycystic kidney.

Other symptoms referring to cardio-vascular system were congestive cardiac failure, pericarditis, abnormal rhythm etc, as given below.

Table 8    Circulatory symptoms in Uraemia

Cardio-vascular symptoms	No. of Cases
Hypertension	45
Congestive cardiac failure	18
Pericarditis	5
Abnormal rhythm	3
Total	52

Out of 18 cases of congestive cardiac failure, 6 cases were admitted as cases of congestive cardiac failure. Uraemia was suspected because patients remained very drowsy or because of urinary changes. Many cases of congestive cardiac failure occurring as a result of hypertension, are really the cases of cardio-renal failure. Renal failure should always be suspected if such a patient remains drowsy. Urine

examination also helps to diagnose correctly the associated renal failure. Urine of cases of congestive cardiac failure should always be high coloured with high specific gravity, whereas if renal failure is associated with cardiac failure, urine will be pale with specific gravity fixed round about 1010. Specific gravity of urine was recorded in 3 cases and it was found to be 1010 in two cases and 1014 in the third case.

Pericarditis was present in 5 cases and helped to diagnose the true condition of uraemia. It is very rare in uraemia of acute glomerulo nephritis but common in uraemia terminating the course of contracted kidney. Out of these 5 cases, 4 cases of pericarditis occurred in cases of chronic glomerulo nephritis, whereas one case complicated a case of nephrosclerosis. It occurs in terminal stages indicating almost invariably that the end is near. Barach found the average duration of life after the discovery of pericarditis to be 29 days, though one of his patients lived for one year. Out of 5 cases of pericarditis lived for 15, 10, 6, 5, and 2 days after the onset of pericarditis i.e., average duration of life after the complication of pericarditis was 7.6 days.

Abnormal rhythm was present in 3 cases—in 2 cases, it was extra-systoles and the third one had gallop rhythm.

*Respiratory Symptoms*—These are quite common in uraemia and may dominate the clinical picture of uraemia. In the late stages of uraemia there is often typical Kussmaul breathing, due to retention acidosis resulting from renal insufficiency. Out of 98 cases, 43 cases had following respiratory symptoms:

Table 9 Respiratory symptoms in uraemia

Respiratory symptoms	No. of Cases.
Marked dyspnoea	21
Haemoptysis	0
Hydrothorax	3
Cheyne-stokes breathing	3
Difficulty in breathing	4
Pain in the chest	-
Total No. with respiratory symptoms	11

Out of 24 cases with marked dyspnoea, 7 cases had dyspnoea as a presenting symptom, so much so that they were treated as cases of bronchial asthma. Three cases were ultimately diagnosed second or third day by the presence of marked oliguria or anuria or suspecting uraemia from the presence of high blood pressure or from urine examination and confirming it by getting the blood chemistry done. Four cases died undiagnosed as cases of bronchial asthma. They were all of the ages between 20 to 35 years. Dyspnoea of renal origin was revealed post-mortem. One of the first 3 cases was seen in the wards by me and is worth reporting. A Muslim boy of 14 years was admitted with an attack of dyspnoea coming on for the first time. There was no family history of asthma. He was treated with inj. of adrenaline, atrophine, and pituitrine without any benefit. Total WBCs count

## SUMMARY

- 1 An analysis of 98 cases of uraemia admitted to KEM Hospital from 1st January, 1934 to 30th June, 1944, is made
- 2 Majority were between the ages of 21 and 60 years
- 3 Chronic Bright's disease was responsible for majority of cases of uraemia
- 4 Symptoms were very varied and belonged to all the systems of the body. In addition, there were skin affections, haemorrhages and generalised anasarca in some cases
- 5 Retinal examination is important to see haemorrhages and to find out the presence of malignant hypertension
- 6 Temperature was normal or subnormal in majority of cases unless infective complications occurred
- 7 Urine examination and non-protein nitrogen and urea nitrogen of blood are the most important diagnostic laboratory investigations for doubtful cases
- 8 Infective complications were mostly terminal and hence of grave prognosis
- 9 Treatment was mainly symptomatic
- 10 Post-mortem findings of 36 autopsies have been recorded

# PRIMARY AMOEBIC ABSCESS OF THE LUNG

## A CASE REPORT

by

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Amoebic abscess of the lung is generally secondary to abscess of the liver but it can occur quite independently of abscess of the liver. The probable route of infection as suggested by C H Burd'ing in 1906 is by direct embolism into the lung through the circulation from the colon. In the sputum generally amoebae are not detected in the primary lung infection. Manson—Baird (1939) writes that probably such cases are of much more frequent occurrence but the difficulty



Fig. 1 Before Treatment



Fig. 2 After Emetine

in obtaining evidence of associated amoebiasis prevents their recognition. In places where amoebic infection is widespread this possibility should always be remembered. One case of primary Amoebic abscess in the lung admitted in the K.E.M Hospital (No S/6179/45) is described below—

A young Hindu male, 20 years old, was admitted in the Hospital on 23rd May 1945 for intermittent fever and cough with expectoration for six months. At the time of admission he was very ill and the main symptoms were acute pain in the lower chest on the right side, cough with expectoration tinged with blood and fever 102 F. A patch of dullness was found at the right base, with diminished breath sounds and few crepitations. Liver and spleen were not palpable. There was no evidence of liver involvement. Fingers showed clubbing. Leucocyte count was 10,000 per cmm. Differential Leucocyte count was—Polymorphs 48, Lymphocytes 47, Large mononuclear 1, Eosinophiles 2. No E. histolytica in cystic or in Trophozoite form were found in the faeces and in the sputum, X-ray showed abscess at the base of the right lung (Fig. 1).

Patient was first treated with adequate sulphathiazole but seeing no improvement after one week's treatment emetine was injected on learning from him that he had suffered from dysentery about eight months ago. There was striking improvement in the condition of the patient after two emetine hydrochloride injections of one grain each. His temperature, after touching normal remained normal without going up again, cough became less and pain in the chest subsided. Since then the improvement in the condition of the patient was uninterrupted. After six injections patient felt still better and was anxious to resume his work as a mill hand. With persuasion he agreed to try in the ward for further treatment. After a total of ten grains of emetine hydrochloride injections he left the Hospital against medical advice. About ten days later he attended the out patient's department when another X-ray plate was taken (Fig. 2) which showed some improvement in the local condition. All these ten days he worked as a mill hand. Since then he has not attended the Hospital so presumably he is well and fit for work.

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# SPINAL TUMOURS

by

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And

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The paper reviews cases of spinal tumours met with at the K.E.M. Hospital from 1940 to the end of July 1945

The operative records of the surgical side show that although laminectomy is being done in the Hospital from its very inception, not a single case of proved spinal tumour has been recorded up till 1940. Since 1940, up to the end of July 1945, we have had 11 proved cases of spinal tumours, apart from one rare case of spinal block.

Of the 12 cases, the youngest person was 12 years of age and the oldest 54, and all the patients in the present series fall in the common age group of spinal tumours. Only one case out of this series, the youngest one, was in a girl. The cases are evenly distributed in the last 5 year period.

The early symptoms in this series have been tingling and numbness in 7 cases, girdle type of pains in 4 cases, shooting pain in 4 cases, and retention of urine in one. These symptoms have been present from a period of one month to eight years—the majority of them, six, coming with symptoms of duration of less than one year. All except one had paraplegia at the time of admission—six being spastic and five of the lower motor neurone type. One case had symptoms of sciatica.

Kahn precipitation test was negative in all cases. Plain X-rays were taken in three cases only, due to shortage of films. Air myelography was done in two cases. But the block was ascertained before operation by Ipiodol in all cases. Lumbar puncture was done in all cases. Five fluids showed xanthochromia.

Out of these twelve cases, six were true neoplasms, four being neurinomas, one meningioma, and one spongioblastoma multiforme. Two were subarachnoid cysts, one of these after removal, showed adhesive arachnoiditis on exploration a year later, and the other one had a primary adhesive arachnoiditis due to high lumbar puncture done for spinal anaesthesia eight years previously. The remaining had vertebral pathology—one being a prolapsed disc, the second hypertrophied ligamentum flavum and the third, the very rare congenital kyphoscoliosis.

In the present series, there was no tumour in the cervical region, seven were in thoracic region and five in the lumbosacral region. Four of these were extradural and seven were intradural, only one was

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A Paper read before the 52nd Meeting of the Staff Society of Seth G. S. Medical College and K. E. M. Hospital, Bombay, on 8th September 1945, with Dr. R. N. Cooper, in the chair.

**Intramedullary** Four tumours were found lying on the posterior aspect of the cord, one postero-lateral and on the left side and one anteriorly. Three were central and three were diffuse, i.e., round about the cord and meninges.

The operation was done under intratracheal anaesthesia. On exposing the dura, the pulsations of the dura were looked for and the region explored accordingly. In two cases only a decompression of the tumour was done and the wound was closed leaving a glove drain.

None of the patients died as a result of the operation. The case of intramedullary tumour, who had advanced cystitis and bed sores prior to his admission, died three weeks after the operation. All the other survived the operation over two months. Four were completely cured, three of them are alive and well today. One died of pulmonary tuberculosis four months after the operation. The remaining were partially relieved of their symptoms. One has not been traced.

In this institution, attempts have been made to diagnose and operate on spinal tumours from its very inception, once in 1926 and again in 1929, without success. These 12 cases of spinal tumours have been detected during the last five years and all of them have been diagnosed before operation when, in most of them, the condition was so advanced that they could not have been missed. Very few investigations were required to diagnose these cases. However, they were made more systematically in more recent cases. As these cases had already advanced degree of spinal compression before the operation, the cure rate is only 25 per cent as compared to nearly 80 per cent or more of other workers whose cases are diagnosed early. Such a result can be obtained by a more systematic investigation of all neurological cases where the clinical picture points to a localised lesion of the spinal cord, or the peripheral nerves and yet does not fit in with the usual known clinical entities. Co-operation between physician and surgeon has been found to be very helpful even in this small experience.

We wish to express our thanks to the Dean of the K. F. M. Hospital for permission to publish this paper. We are grateful to Dr. N. K. Sahar and Mr. R. N. Cooper for their encouragement and allowing us to study these cases.

#### DISCUSSION

Dr. N. K. Sahar mentioned that his first case of spinal tumour was clinically diagnosed by him as sub-acute combined degeneration but on further investigation this diagnosis proved to be wrong. Similarly he quoted two other cases—one in the Parsee General Hospital and the other in the Wadia Children's Hospital which were missed in the beginning. He enquired why lipiodol should be left last in the list of investigations.

Dr. L. H. Athale emphasized the necessity of being conscious of spinal tumours as an entity—as in the U. S. A. these tumours were diagnosed very frequently.

Dr. I. Monteiro reported one case from the autopsy record of the K. F. M. Hospital obtained from a total of 5,500 autopsies. He observed that this was a small figure compared to that of Schlegel in Vienna who had reported 44 tumours of the cord and meninges in 25,000 autopsies. This small number was due to the fact that the spinal cord was not opened as a routine in the autopsy room for want of adequate time.

N. H., age 35 years, male was admitted for inability to use all the limbs, duration four days. On examination power was diminished and the tone increased in all the limbs. Superficial sensations impaired, deep sensations normal. The deep jerks were exaggerated, plantar extensor right side, abdominal and cremasteric absent. The ankle clonus was present. There was incontinence of urine and stools. The spine and the skull were normal. B.P. 150/110 mm Hg. C.S.F. obtained by lumbar puncture showed Troin's syndrome. The fluid from the cisterna magna was under pressure. Protein 0.06%, Globulin and Sugar normal. 2 cells per c mm being lymphocytes. The patient developed basal crepitations, a bed sore and hyperpyrexia. Ascending lipiodol of the spine showed blockage at the lower cervical region. The patient expired six months after admission. At the post-mortem examination the vertebral column was opened to reveal a soft, pedunculated vascular extrathecal and antero-lateral tumour arising at the level of the body of 7th cervical vertebra extending upwards.

to the 4th and below to the 7th cervical vertebrae. This tumour had produced an indentation of the spinal cord. On cutting through this tumour a whorled appearance was seen. Histologically the tumour showed characters of a neurofibroma. The brain was normal though there was an increase in the C S Fluid. The other findings were basal collapse of lungs, a fatty liver and ascending pyelonephritis.

Dr K A J Talaka quoted a case of spinal tumour operated upon by Dr Max Peet in America in 1945 a month following the laminectomy a marked improvement was observed.

Dr R G Dhayagude said I must congratulate Drs Cooper and Ginde on their excellent paper on spinal tumours. Dr Monteiro has already mentioned our difficulties in the post mortem room. I should like to point out one condition which simulated a growth viz., syringomyelia. I had an occasion to do a post mortem in which a tumour was suspected and on opening the spinal cord small, irregular cavities were found about the central canal.

Dr R G Ginde replying to Dr Salidar's question as to why lipiodol should not be used, said that almost the same information can be obtained from the other simple tests such as a plain X rays of the spine and manometric tests and secondly lipiodol does produce irritation of the meninges sometimes leading to aggravation of symptoms and might ultimately get on cysted and produce a condition of lipiodosis. He further said that when no tumour is detected as shown by the lipiodol going down to the bottom of the spinal canal the lipiodol required to be removed to avoid the above complications.

Dr R N Cooper in his concluding remarks said that in the diagnosis of spinal tumours it should be remembered that patients are likely to forget their 'root pains'. A certain length of time passes between the disappearance of pain and the appearance of some patch of anaesthesia and the patient may not give a clear history unless he is interrogated from that point of view. As regards paraplegia in flexion he pointed out that in the early stages the patient may find a certain stiffness in locomotion with the onset of flexion paraplegia. The patient finds that one leg suddenly gives way and he falls down. He pointed out that there were some fallacies in connection with the lipiodol test. It has happened that the needle has slipped out from the dura and the lipiodol is deposited into the epidural space. He asked for closer co-operation between the Physician and the Surgeon in the final assessment of a neurological case.

## Book Reviews and Notices

THE MEDICAL ANNUAL, 1945, 63rd year. Edited by Sir Henry Tidy and A Rendle Short. Bristol: John Wright & Sons Ltd., 25 S. Pp. 410.

This useful annual maintains its usual standard in reviewing the publications of the previous year from the general practitioner's point of view. The new sections on measurement of morbidity, vital statistics, and mass miniature radiography, will we hope become regular features of this publication. The full articles on atypical primary pneumonia, cutaneous leishmaniasis, poliomyelitis, cirrhosis of liver, penicillin will prove of special interest to our readers.

## Obituary

**BACHA, ARDESHIR PESTONJI** born at Navsari (Baroda State) in 1881, died at Bombay May 5 1945 aged 64, of *Carcinoma of Pancreas*. Educated at Navsari High School, Grant Medical College 1908 (L.M. & S. 1903), and University College Hospital Medical School London M.B.B.S. Lond. 1907 F.R.C.S. (Eng.) 1909 private surgical practitioner in Bombay since 1910. Hon. Surgeon and Lecturer in Surgery, G S Medical College and K E M Hospital Bombay 1926 to 1930. Examiner in Surgery University of Bombay and College of Physicians and Surgeons of Bombay. President of Bombay Medical Union. A brilliant and successful surgeon popular teacher and staunch nationalist. Has left his valuable collection of medical books to C S Medical College Library.

**SHAH, TRIBHOVANDAS OGHADDAS**, born at Vadnavan (Kathiawar State) on July 1 1888 died at Dharwar while on a holiday on November 2 1945 aged 57 of *Coronary Occlusion*. Educated at Vadnavan High School and Grant Medical College (L.M. & S. 1912) I.R.C.P. 1913 F.R.C.S. (Eng.) 1920 F.C.P.S. (Bomb.) Worked as Hon. Surgeon to Peoples Free Hospital II N Hospital B G Hospital K E M Hospital and C S Medical College and Jeebhai Wadia Hospital for children. Examiner in Surgery for M.B.B.S. and M.S. University of Bombay.

**MOOS, FRAMROZE NANABHAI** born in Bombay, on 22nd August 1893 died in Bombay on Aug 7 1945 aged 52 of *Carcinoma of the Stomach*. Educated at Grant Medical College (M.B.B.S. 1915) and University College London M.B.B.S. (1920) M.D. (1922) D.T.M. & H. (1920) D.P.H. (1920) Bombay Medical Service First Class, Examiner in Medicine, University of Bombay Superintendent Goculdas Tejpal Hospital, Bombay, (1924-1945).

**DUDHA DINSHAW HORMUSJI**, born in a village near Navsari (Baroda State) on September 12 1899 died at Bombay on January 14 1945, aged 46, of *Coronary occlusion and diabetes mellitus*. Educated at Navsari High School (1916) and Samaldas College, Bhavnagar (1917) and Grant Medical College Bombay (1917-1922) M.B.B.S. 1922 M.D. 1925 M.R.C.P. (Lond.) 1926 I.C.P.S. (Bomb.) 1938 obtained University Cash prize of Rs 200 in intermediate M.B.B.S. examination F M Shah Silver medal Farish Scholarship Cowasji Jehangir prize, Reid Scholarship in midwifery Balkrishna Sudamji Prize and MacLennan Scholarship, Silver Prize Medal and P B H Nanavaty Book Prize at the final M.B.B.S. Hon. Physician Parsi General Hospital 1926, Bai Y L Nair Hospital 1928-1945 and Jeebhai Wadia Children's Hospital 1929-1945 Principal National Medical College 1936 to 1945 Active member of the Bombay Medical Union Vice President of the State Medical Faculty 1943-1945.

**VORA, JETHALAL VANMALI, L. M. & S. (1908)**, died of *Intestinal Tuberculosis*.  
**PALAKHIWALA, KAIKHUSHRU BAMANJI, M.B.B.S. (1921)** died of *Coronary Occlusion*.  
**NANAVATI, B P, M.B.B.S. (1918), D.O.M.S.** died of *Tuberculosis*.  
**MEHTA, SIR MANGALDAS V, (1884-1945)** O.B.E., I.M. & S., F.R.C.P.I., F.C.P.S. died of *Pernicious Anaemia*.

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